SAJOUS S ANALYTIC CYCLOPEDIA OF PRACTICAL MEDICINE

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Preface

THE purpose of this Service Volume is to make available to the medical profession a critical review of the noteworthy accomplishments in Medicine, Surgery and the various Specialties that have marked the past year. In this volume no attempt has been made to furnish a complete bibliography of medical literature for this period. The value of a review of this kind depends upon the discriminating judgment and ability of the reviewers. The Editorial Board responsible for this volume, itself thoroughly experienced in the production of such a work, is fortunate in having had the aid of a group of contributors who are not only outstanding in their respective fields of medical endeavor but are reliable critics who have a clear understanding of the needs of the general practitioner.

The material contained in this volume has been arranged in a concise and readily available form which should render it of additional value to those who depend upon this Service Volume for their information on the progress of medicine. Under the main headings of Medicine and Surgery will be found the generally accepted subdivisions of those subjects. These are followed by sections devoted to Obstetrics, Pediatrics, Ophthalmology, Otorhinolaryngology and the other well recognized specialties.

Throughout the volume, treatment is emphasized. Therapeutics is dealt with in its broadest sense, special sections being devoted to Physical Therapy, Psychotherapy. Dietotherapy as well as to the Newer Drugs. Under the latter heading will be found an adequate discussion of Sulfanilamide and its allied compounds that bid fair to revolutionize the treatment of many acute infections as well as pneumonia. The chapter on Dietotherapy is of unusually practical value because of the number of specific diets that are included. The rapid and ever changing status of Endocrinology is carefully discussed. The steadily increasing information about vitamins is critically analyzed.

Surgery in its various phases, but more especially Abdominal Surgery, as always, is accorded a prominent place in this Service Volume. Modern anesthesia, the present conception of cancer, the various advances in endoscopy and radio-therapy, peripheral vascular disease, the various forms of shock treatment now employed in neuropsychiatry are all accorded special consideration not to mention innumerable other subjects of equal contemporary importance that are carefully discussed

iv PREFACE

The publishers are to be congratulated upon the pleasing appearance of this volume which is illustrated with unusual generosity. The thanks of the Editor are due to Dr. Edward LeRoy Bortz who is entirely responsible for planning this volume and supervising its publication. We are indebted to Dr. Frederick C. Smith for his careful preparation of the manuscripts and for seeing the book through the press.

The Editor deeply appreciates the whole-hearted and enthusiastic co-operation of the Editorial Board and the various contributors. We believe that this Year Book will amply fulfil its purpose and we hope that it will prove of value to the medical profession of this country.

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The Cyclopedia of Medicine

Revision Service—1940

MEDICINE

Edited by George Morris Pifrson, B.S., M.D.

and

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ALLERGY

By HARRY BOND WILMER, M.D., and MERLE MIDDOUR MILLER, B.S., M.D.

TREATMENT OF INTRACTABLE ASTHMA

Epinephrine—Epinephrine in Gelatin—In patients who have been taking repeated doses of the 1:1000 aqueous solution of epinephrine at frequent intervals, we have found the use of epinephrine in gelatin very desirable. We use the gelatin preparation almost always when indicated instead of the epinephrine in oil, the original "slow epinephrine" Both epinephrine in oil and in gelatin are absorbed much more slowly than the aqueous epinephrine which is often fleeting in effect although very beneficial for a short time

W. C. Spain, M. B. Strauss and A. M. Fuchs¹ first prepared a solution of epipephrine in gelatin which delayed the rate of absorption and lengthened the period of influence on the patient.

Kolm and Bulger have reported that zinc slowed the absorption of epinephrine but almost immediately oxidized it, diminishing the effect of the epinephrine

Gelatin is nontoxic, nonantigenic and reasonably stable. It is well suited as a

vehicle to delay the absorption of epinephrine because of its nonantigenicity. A bacterial growth factor was noted in some gelatins but is decidedly inferior in Eastman photographic gelatin. It was found by Koser, Chinn and Saunders² that the growth-promoting effect was highest with 5 per cent gelatin. 10 per cent, and 15 per cent concentrations were inhibitory. The gelatin used in the preparation of the gelatin epinephrine mixture is 16 per cent. The method of preparation as devised by Spain and his coworkers is as follows:

To a solution containing 11₃ ounces (40 cc) of glycerin and 41₃ ounces (130 cc) of distilled water, are added 27 grains (1.8 cm) sodium chloride. 15 grains (1.9 cm) chlorobutanol, 3 grains (0.2 cm) sodium bisulfite and 11₃ ounces (40 cm) gelatin. The gelatin is added last and the preparation is mixed vigorously by rotation. This quantity of gelatin is conveniently made in a 1-quart (liter) pyrex. Florence flask since the mixture tends to boil over if it is sterilized in too small a container. The

(1)

gelatin preparation is sterilized by autoclaving for 30 minutes at 20 pounds pressure. Aerobic and anaerobic cultures are made and kept at 98.6° F. (37° C.) for 4 days before the sterility of the mixture is decided upon or the gelatin mixture dispensed for use. This gelatin mixture remains stable for months if kept in the refrigerator. The 1:500 epinephrine solution used in this preparation is made by adding to 4 parts of the above sterile gelatin mixture, 1 part of 1:100 epinephrine solution Aseptic precautions should be followed when the epinephrine is added and in the subsequent method for bottling. The gelatin mixture must be warmed in hot water to liquely the gelatin so that it may be pipetted accurately. This 1:500 gelatin epinephrine solution is dispensed in sterile brown bottles.

This mixture is a gel at room temperature as well as at the lower temperature of the refrigerator (41° F--5° C) in which it should be stored. For administration it must be liquefied by warming. This is most easily accomplished by placing the vial in a container and covering it for a few minutes with a portion of the hot water in which the syringe has been boiled. The syringe is kept warm while the gel is liquelying by allowing it to stay in the remainder of the hot water. Since the preparation is given subcutaneously rather than intramuscularly, it may be self-administered, the usual allergy syringe and needle (tuberculin type syringe and 26 gauge 12 inch needle) being used No untoward effects have been noted other than an area of moderate irritation at the site of the injection, occurring in the occasional patient and lasting no longer than 24 hours

The dosage given was from 5 to 15 minims (0 3 to 1 cc.). The latter dose usually allowed the patient to sleep through the night

M. M. Miller³ reported the use of epnnephrine in gelatin in over 100 cases. Only 1 untoward reaction was noted and this consisted of pallor, marked perspiration, and tremor after a small amount of the gelatin was injected intravenously unavoidably.

It is always well to advise the patient to draw back on the plunger several times while administering the solution.

Spain did not report any unpleasant side effect other than usual pallor, etc., which is encountered with the use of aqueous adrenalin.

We feel that the gelatin epinephrine solution is the mixture of choice when prolonged effect is desired for the following reasons:

- 1 It is nontoxic and nonantigenic
- 2 It is solution and not suspension
- 3 It is easily self-administered by subcutaneous injection in contrast with the oil preparation of Keeney which must be given intramuscularly
- 4 It is not necessary to have a dry sterilized syringe
- 5 In using both the gelatin and oil preparations, a definite reduction is noted in the number of doses required daily by a patient

Epinephrine in Oil — As has been stated above, we believe that the gelatin epinephrine preparation has certain advantages over the suspension of epinephrine in oil but a large number of physicians are obtaining splendid results with the oil epinephrine

E L Keeney has reported the results of his observations in a preliminary report and later the above author with J A Pierce and L N Gay⁵ reported more clinical findings Epinephrine in oil or "slow epinephrine" is a suspension of powdered epinephrine in peanut oil It is best administered intramuscularly in the deltoid or gluteal muscle, especially if repeated injections are to be given Occasional doses can be given subcutanoeusly in the buttocks

In patients with acute attacks of asthma, it is often well to give a preliminary dose of the aqueous solution of epinephrine hydrochloride and follow later with a dose of epinephrine in oil. The average adult dose of "slow epinephrine" is 15 minims (1 cc.). If the attack is severe, 22 minims (1.5 cc.) may he given. It has been our experience that, at times, the "slow epinephrine" acts almost as quickly as the aqueous solution and also that doses smaller than 15 minims will sometimes be sufficient. The average dose for a child from 2 to 5 years is 7½ minims (0.5 cc.); from 5 to 12 years, 12 minims (0.75 cc.).

Both the suspension in oil and the solution in gelatin can be used in the treatment of severe cases of urticaria and angioneurotic edema. The dosage is the same as that given in the treatment of bronchial asthma, 7½ to 22 minims (0.5 to 1.5 cc.), depending upon the severity of symptoms and the patient's tolerance to epinephrine.

Epinephrine by Inhalation—Better results are being obtained lately from the use of 1 100 solution of epinephrine by inhalation. The reason is that more efficient glass atomizers are manufactured which deliver a larger amount of finer spray to the bronchial mucosa. At times, it should be given at regular intervals, ie, every 2 or 3 hours for 24 or 48 hours, with the hope of possibly building up an "adrenalin reserve" and breaking the asthmatic cycle. It may be given more frequently if the occasion arises The use of an inferior atomizer may produce unpleasant and annoving dryness of the throat and, at times, gastrointestinal upsets from contact of the strong solution with the various mucous membrane surfaces

J B. Graeser and A H Rowe⁶ have obtained beneficial results in the treatment of bronchial asthma by the inhalation of a solution of epinephrine 1:100, For the spray, an atomizer should be used which vaporizes the solution to a degree sufficiently fine so that the particles will be disseminated to all parts of the lungs. The dosage varies with the patient and at the beginning it is a "trial and error" method. Caution must be observed, but the only untoward symptoms noted have been severe headaches from prolonged use and a dryness of the throat. Only rarely have we noted any constitutional reactions. It is well to allow several minutes to elapse between deep inhalations. In a great many instances the use of the 1:100 solution by inhalation has supplanted the hypodermic injections of the 1:1000 solution. As a prophylactic, it is suggested that repeated inhalations during the free period of the day may prevent recurrent attacks or mitigate the severity of any paroxysm that might develop.

Electrophoresis of Epinephrine into the Skin—It has been known for years that epinephrine may be transported into the skin where it produces the typical blanching of the dermis. A method for administering epinephrine by this method has now been developed

The epinephrine solution is applied on cotton or canton flannel. The area of application on the arm or the leg is usually 30 cm. Two or 3 areas are used in each treatment which lasts for 10 to 15 minutes. The blanching usually lasts about 5 hours without injury to the skin. The rate of absorption is retarded by the blanching itself. The epinephrine is slowly released from its depots in the skin and its action prolonged.

The effects of administration of epinephrine were the same as those when giving epinciphrine by the usual methods. Benefit was derived in most of the cases reported and in some, the usual untoward nervous symptoms were noted. At times

it was necessary to give the patient an injection of epinephrine even though he had had epinephrine by iontophoresis. It is the opinion of the men who have done this work that further developments in this technic may give us a means of administering epinephrine which will give us a more prolonged and effective action.

Intravenous Epinephrine—I. S. Kahn⁸ presents 16 cases, all desperately ill, and in all of whom hypodermic injections of epinephrine in the usual doses were of absolutely no effect in relieving the asthmatic paroxysm. He believes that, when this drug in doses of the usual size have failed, its further indication and efficiency can better and more safely be determined, not by increasing the dose given hypodermically, but by proceeding cautiously intravenously. He suggests the use of a 1:1000 dilution in doses of 2 to 4 minims (0.13 to 0.26 cc.), using a tuberculin syringe and a 26-gauge needle. We suggest diluting this amount in 10 cc. normal saline. He states that, even if given in such small doses and slowly, this is an extremely shocking measure, terrific pallor, tremor, sweating, headaches, heart pounding and, at times, terrific nausea and vomiting occur almost He has never seen a patient instantly who has failed to develop either some or all of these symptoms. It is felt that some of these untoward reactions can be avoided or reduced by using a 1.10,000 solution. We feel that the administration of epinephrine by the intravenous method should be used only in extreme cases, very cautiously and in minute doses

Untoward Reactions of Epinephrine—The aqueous solution of epinephrine is still the "drug of choice" in acute asthma. The best and most efficient results are obtained if the dose is given early, before marked bronchial edema and profuse secretion of mucus take place.

Many patients do not tolerate epinephrine well and for this reason we believe it is best to begin with 1½ to 3 minims (0.1 to 0.2 cc.) the first time the drug is given, as reactions are quite common. The symptoms are tremor, pallor, nervousness, palpitation, and cardiac distress. Also in many instances, these small doses will produce the same effect as larger doses. After the patient's tolerance is determined, the doses given should be governed by the severity of the attack. Epinephrine is not habit forming and may be used over a long period with safety.

There is no substitute for epinephrine in constitutional reactions following the injection of pollen extracts or sera. This preparation should be kept close at hand when any solutions, that at times produce anaphylactoid reactions, are given.

Often severe, intractable, chronic asthmatics build up a tolerance to adrenalin. The dose is gradually increased and still no effect is obtained. At this time, other measures must be taken

J Cohn⁹ feels that the use of epinephrine in the oily suspension is not without unpleasant, if not potentially serious, complications He reports 4 experiences with severe untoward reactions half hour after the routine dose of 4 minims (0.25 cc.) of 1:1000 aqueous solution of adrenalin was given, 15 minims (1 cc) of a solution of $\frac{1}{30}$ grain (20 mg) of epinephrine crystals in peanut oil were injected intramuscularly into the deltoid muscle, care being taken to pull back the plunger to make sure the oil was not being injected into a vein. The untoward symptoms noted in these patients were pallor, nausea, vomiting, sweating, cyanosis, and thready pulse and increased dyspnea. Severe local itching and angioneurotic edema at the site of injection followed in 3 of the 4 cases reported The authors of this section

know of only 1 untoward reaction to epinephrine in gelatin, this being due to injecting a small amount into a vein or capillary bed. We have noted several local reactions from epinephrine in peanut oil.

Smith and Paul¹⁰ point to the fact that they have seen at least 1 case in which epinephrine had a deleterious effect on the patient's cardiovascular system. Our experience has been that epinephrine rarely does any damage to the heart or vascular system. We have had the opportunity of observing 7 asthmatics at autopsy and in none of these was there any evidence of cardiac damage. Several of them had been taking large doses of epinephrine repeatedly. In 1 case the coronary vessels were injected with mercury and x-rayed and no coronary disease could be detected

We feel that during prolonged bronchial asthma, myocardial damage should be looked for especially if the patient is taking frequent doses of epinephrine. The drug should always be used in as small a dose as possible. Colton and Ziskin¹¹ have shown that in chronic bronchial asthma with associated emphysema there is frequently a tendency to myocardial involvement.

Coca¹² feels that the heart is usually injured only very slightly Kountz, Alexander and Prinzmetal¹³ have shown in their investigations that in most chronic asthmatics there is definite right ventricular strain

In patients with hypertension, epinephrine is not usually contraindicated if other drugs have failed. We have seen patients who have had high systolic pressures which have been actually reduced by the relief of the asthmatic attack by an injection of epinephrine. Small doses should be used and careful, frequent blood pressure readings should be taken in all hypertensive individuals. We look

on the use of epinephrine in hypertensive patients as the lesser of 2 evils.

Ephedrine — Ephedrine acts very much more slowly than epinephrine and its only advantage is that it is efficacious by mouth. The usual dose is from % to ¾ grains (0.0243 to 0.0486 Gm.). Frequently, untoward nervous symptoms develop after the use of this drug and for this reason barbiturates often are incorporated in a capsule or tablet with the ephedrine. We usually use ¼ to ½ grain (16 to 30 mg.) of phenobarbital; amytal, ¾ grain (50 mg.); nembutal, ½ grain (30 mg.); seconal, ½ grain (30 mg.); or any of the other commercial products, using a corresponding dose.

Several synthetic ephedrinelike preparations have been put on the market. J. A. Murphy¹⁴ has reported a series of cases treated with *propadrin* and he believes that the dose should be the same as that of ephedrine Our experience has been that it is usually necessary to give twice as much propadrin as ephedrine to obtain similar results. The advantage of this preparation is that it precludes all the side nervous effects often seen when giving ephedrine Propadrin can also be given in conjunction with the barbiturates

We have treated between 40 and 50 cases in our clinic with a combination of propadrin, ½ grain (30 mg.), and theophylline, 4 grains (026 Gm). This combination was found especially effectual in bronchial asthmatics with associated cardiovascular damage and in elderly patients. We have maintained a large percentage of these patients in a very comfortable state for long periods by 3 or 4 doses of the above combination, 3 times daily after meals and at bedtime. Some of these patients were taking frequent injections of epinephrine and, while using the propadrin-theophylline preparation, were able to reduce the

number of daily injections Four patients were able to stop epinephrine entirely. We suggest the use of propadrin and theophylline in chronic asthmatics who have daily wheezing and coughing and especially in those who have some evidence of poor coronary circulation.

Other Medication in Asthma -Morphine is a drug which must be used with extreme caution in asthmatics. It frequently gives a patient the bronchial relaxation and necessary cardiac rest but at the same time it is depressing to the all important cough reflex. It is also a respiratory depressant. Deaths have been reported after the use of morphine in patients in status asthmaticus They have been relieved for a time but after a prolonged rest and relaxation they have awakened filled with thick tenacious mucus, unable to cough and, unless drastic action is taken, they will be asphyxiated. We have seen this mechanism in 2 cases, 4 to 5 hours after the administration of morphine

The above precautions apply to other opiates, such as *dilaudid* and *pantopon*. We have used these and morphine in some cases with beneficial effect. Frequently an allergic individual will have an idiosyncrasy to opiates and this is another reason for using caution when thinking of using morphine and the opium derivatives.

Atropine gives bronchial relaxation and dilatation but at times has an unpleasant drying effect on the secretions and renders the tenacious mucus in an asthmatic chest even more mucilaginous. It is often well to use it with the first dose of morphine. Subsequent or alternate doses of the opiate can be given without the atropine if morphine must be used.

The barbiturates, bromides, and other sedatives may be used when indicated, especially if a patient is very

apprehensive and nervous. Care must also be exercised in the use of these drugs as asthmatics at times are hypersensitive to these as well as to other drugs. It is often best to start with small doses and increase to a therapeutic dosage later. The above drugs often go a long way in aborting an attack by doing away with the neurogenic factor. This element is often of great importance in precipitating and continuing an asthmatic seizure.

Acetylsalicylic acid (aspirin) in the usual dose and combined with other drugs may and often does give relief. The exact mechanism of action is not explained but its promiscuous use in allergy is very dangerous as we have observed many allergic individuals who have a marked idiosyncrasy to this drug. Several times, severe constitutional reactions have been encountered. It is always well to inquire if the patient has previously taken aspirin with no ill effects. Any of the coal tar series may give untoward symptoms.

Calcium, orally or intravenously, has been used in many or all allergic diseases. This drug is readily absorbed and tolerated in the gastrointestinal tract, so usually there is no need to administer it by any other route. It is very much of a question whether any allergic symptoms have been markedly relieved by calcium. The usual preparations are calcium lactate and gluconate, 10 to 15 grains (0.6 to 1 Gm.) 3 to 4 times a day.

Waldbott¹⁵ first reported the use of aminophylline (theophylline with ethylenediamine) in emergency treatment in asthma. He found this drug was particularly efficacious in the so-called "adrenalin-fast" cases. We have used aminophyllin by mouth in a great many patients with bronchial asthma who are not in status asthmaticus. It seems to be beneficial especially in those who have

some myocardial damage and poor coronary circulation.

G. T. Brown¹⁶ believes that aminophylline intravenously has proven of definite benefit in cases of status asthmaticus and may at times be a lifesaving measure. He recommends a dosage of 7.5 grains (0.5 Gm.) of aminophylline in 4½ to 5 drams (18 to 20 cc.) of 50 per cent glucose and he injects the mixture slowly.

Iodized oil can be administered in several different ways, i. e., (a) the intravenous catheter, (b) gravity method, which is accomplished by pulling the tongue forward and allowing the oil to run down, (c) intratracheal instillation by a laryngeal syringe (this technic is described by R. M. Balyeat, L. E. Seyler and H. A. Shoemaker¹⁷) and (d) bronchoscopic application which some workers contend is by far the best method. For practical and routine use, it is felt that instillation by the laryngeal syringe is the most desirable means of administration.

Untoward reactions observed from the use of iodized oil are as follows Iodine sensitivity and iodism, Balyeat reports as a possibility. We have had 1 case in which quite marked edema and inflammation of the respiratory mucosa followed the instillation of the oil Subsequently this patient was proven highly sensitive to iodine preparations. W Anderson¹⁸ observed severe iodism in 8 (b) Convulsive cough often follows the introduction and there is a possibility of massive collapse of the lung or a lobular atelectasis. (c) Criep¹⁹ encountered the following distressing symptoms. Severe dyspnea, cvanosis, and circulatory failure from which the patients recovered Plehn reported 1 case of traumatic bronchiectasis following a prolonged convulsive cough. (d) Pneumonia developed in 8 of Anderson's cases and all but 1 recovered. Other workers report oil in the lungs for months to years after instillation. (e) Allergic reactions characterized by urticaria, asthma, arthritis, and fever have been referred to by different observers. A sensitivity to the oil used as a vehicle for the iodine is thought to be a factor in some cases.

Fatal termination to complications resulting from the use of the instillation of iodized oil is not rare and Criep feels that all the disadvantages and possible untoward reactions noted above should be carefully weighed before treatment of this type is instituted.

Potassium, sodium and strontium iodide in doses of 5 to 15 grains (0.3 to 1 Gm) 3 times daily is probably the best alterative and liberator of bronchial secretion at present available. Some allergic individuals cannot tolerate therapeutic doses, but this preparation is worth a trial in all asthmatics, especially of the intrinsic or mixed type.

Bray,²¹ Black, and others have used glucose intravenously in acute attacks in doses of $\frac{2}{3}$ to $1\frac{2}{3}$ ounces (20 to 50 cc.) of a 50 per cent solution. It may be given every 4 to 6 hours and then once or twice daily until the patient is well able to take sufficient carbohydrate by mouth these cases, the carbohydrate metabolism perhaps is normal but the patients, being cachectic and undernourished, are in need of this form of concentrated nourishment If the patient is dehydrated, a 5 to 10 per cent solution in larger doses may be given slowly over a longer period of time if indicated Some workers²² have been using a 50 per cent sucrose **solution** in dose of $1\frac{2}{3}$ ounces (50) cc). This probably has a more prolonged effect and is possibly more dehydrating and seems to give better results. L. N Gay²³ recommends this form of carbohydrate intravenously and has treated many cases with this preparation

Helium-oxygen Therapy in Bronchial Asthma-The use of helium mixed with oxygen, in bronchial asthma, was reported in 1934 by Barach.24 Because of the physical property of lightness, helium carries the oxygen into spaces and orifices much smaller than the nitrogen-oxygen mixture can go. It is moved through these openings at about one-half the pressure required by air At the present time, the usual mixture employed is 20 per cent oxygen and 80 per cent helium.²⁵ This combination can now be purchased together in this concentration in the same tank. If a leakproof oxygen tent is available, this can be used, but the flow of the mixture at 30 liters per minute is quite expensive and wasteful and at the present time the face mask, either nasal or oral-nasal, is advised.

This mask can be placed over the face at intervals or can be strapped to the face with adhesive. A special adapter with a helium-oxygen gauge is necessary and the flow is usually from 6 to 12 liters per minute. Usually about 8 liters per minute allows a patient to breathe quite comfortably. The inhalation of the helium-oxygen mixture makes possible a more normal gas velocity movement with much less effort for the reason that this mixture is especially efficacious and applicable to patients in status asthmaticus and chronic asthma with excessive and marked emphysema.

The cost of helium is gradually being reduced and for this reason it is more available than before. Also the combination of helium and oxygen in the same tank to be used with a special adapter renders the use of 20 per cent oxygen and 80 per cent helium much simpler

Bronchoscopy — Bronchoscopy has been done both as a diagnostic and therapeutic procedure. It is frequently employed in differentiating between foreign body and asthma in children. It has aided at times in determining the presence of a bronchogenic carcinoma which did not show on x-ray examination of the chest.

As a therapeutic aid this procedure has proven invaluable in patients with bronchiectasis and also in the collection of mucus and secretions from the bronchi for the preparation of autogenous vaccines. Repeated drainages often benefit greatly an asthmatic with a large number of thick tenacious plugs which recur frequently.

In status asthmaticus, it is often very difficult to do a bronchoscopy, but in selected cases which apparently have the bronchial tree almost completely occluded with mucus, this procedure has given marked relief.

Prickman and Moersch²⁶ have used bronchoscopy in patients who have bronchostenosis both diagnostically and therapeutically. The "stenosed bronchus" can be readily dilated and retained secretions aspirated Repeated drainages have to be done on some cases.

Surgery—The treatment of intractable bronchial asthma by bilateral resection of the posterior pulmonary plexus is reported by Rienhoff and Gay 27 Only patients totally incapacitated physically were selected for this procedure Physiologic observations have shown that bronchoconstrictor fibers are distributed mainly in the branches of the vagus nerve to the lung of the same side and that of the opposite side and to some extent accompany the sympathetic fibers Pronounced narrowing of the air passages has been produced experimentally by stimulating the proximal and distal ends of the divided vagi and sympathetic trunks as well as the intact nerves.

The rationale of the resection of the posterior pulmonary plexus is based on the fact that the extrinsic nerve supply

of the lungs consist of 2 separate and independent tracts. The cells of origin of the vagus sensory tract lie in the ganglion nodosum to which run fibers from the trachea and lungs. Stimulation of the central trunk of the cut vagus or the intact vagus incites reflex narrowing of the bronchi. There is a double nerve supply to each lung, the course of which is through both the sympathetic and parasympathetic or vagus trunks.

Results obtained by the resection of the posterior pulmonary plexus have been fairly encouraging. This procedure is not recommended in patients with marked pathologic change or with advanced cardiac disease The authors recommend a very careful allergic, medical and cardiac study before a procedure as radical as this is tried.

Irradiation—C. K Maytum and E. T. Leddy²⁸ in 1936 reported their results on the treatment of refractory bronchial asthmatics by the use of x-rays Their report at that time included 23 cases These same authors report this year the results obtained in treating 161 patients with moderate and severe bronchial asthma. Twenty-four per cent obtained marked relief Moderate relief was noted in 16 per cent and 14 per cent obtained marked relief, but other treatment given at the same time may have been the more important procedure Forty-six per cent of these patients had less than 50 per cent relief and were classed as failures

Roentgen therapy does not replace the usual treatment given an asthmatic but at times it is a valuable adjunct in the treatment of intractable cases. Also the warning is given that it should not be used indiscriminately as considerable harm may follow overdosage or too frequent use. The beneficial results from x-ray treatment are often only temporary and not a curative measure. The formula given by the authors is as follows:

kv. 135; filter 6 mm. A1; distance 40 cm.; ma. 5; time 25 minutes = 500 R.

Irradiation at first was given over the mediastinum through 2 paravertebral fields. Later they have been using the anterior and posterior fields in the mediastinum but it is possible that the latter method is harder on the patient and probably produces no better results. Epinephrine is often given just before or during the treatment.

Maytum²⁹ gives the following opinion of x-ray treatment: "Any qualified roent-genologist, however, should know the dosage that the skin will tolerate and the interval at which it can be repeated. Also, treatment should be given only by such a qualified roentgenologist. The recommended dosage should not do harm if the intervals are a month or more apart and if treatment is not repeated too frequently."

Rest—A hospital is the ideal place for complete relaxation and rest. It has been the writers' experience in many cases that hospitalization per se was enough to give a patient complete relief without any medication, hyposensitization, etc Improvement practically always follows continued rest, both physical and mental Complete rest is the first and most important part of any acute asthmatic regimen

Piness once made the statement that if the individual in status asthmaticus is given complete physical and mental rest, plus fluids, he will usually come out of the attack in good condition. As we have previously stated, there are many adjuncts in the treatment of bronchial asthma but, first and most important, is complete rest.

B. A. Credille³⁰ stresses the importance of rest in the treatment of allergic diseases Fatigue and exhaustion are very vital secondary factors and, as has been found, often the most important

mechanism in precipitating an attack. He believes that an allergic individual has a definite fatigue threshold. When this is lowered, the patient is more likely to have an attack. Prolonged rest is a most valuable adjunct in the treatment of asthma, asthmatic bronchitis, and the like. This is especially true of the "high strung" nervous type of patient.

POTASSIUM SALTS IN ALLERGY

H. A. Rusk and B. D. Kenamore³¹ treated a small series of cases of urticaria with a high protein, low sodium, acid-ash diet. They added to this, potassium chloride in doses of from 60 to 90 grains (4 to 6 Gm.) daily. They felt that there was a sound physiologic and therapeutic basis in that these individuals suffering from urticaria and angioneurotic edema had an altered mineral balance. It was through the work of Nathan and Stern that there was found a low serum potassium level in certain dermatoses. Klauder and Brown³² reported a direct relationship between the serum potassium and skin irritability Other observers have shown that pharmacologically potassium at times produces a reaction almost analogous to that of epinephrine

This group of patients was observed clinically only and no laboratory determinations of significance were done. The diet given was made up mostly of proteins, vegetables and noncitrous fruits. No salt was served with meals but potassium chloride was used instead of sodium chloride. The Caloric value of the diet was arranged to suit the patient. In brief, the diet is as follows.

Fruits—Noncitrous, fresh or stewed Vegetables—Especially beets, carrots, Brussels sprouts, corn, lettuce, mushrooms, peas Meat and eggs twice daily.

Milk—One glass and ½ glass of cream.

Salt-free butter.

Bread, cereal and starches—a limited amount.

Following the therapeutic approach of the above workers, R. E. Cohen³³ reported a small group of cases in which he used a high protein, low sodium acidash diet. Rusk and Kenamore treated 6 patients.

In 8 cases treated in the same manner, no improvement was noted during or following the régime and the benefit derived from this therapeutic approach seems doubtful.

B. Bloom³⁴ reported striking results from the use of potassium chloride in hay fever He gave much smaller doses than previously reported. Instead of 15 grains (1 Gm.) every 4 hours in enteric coated capsules, 5 grains (0.3 Gm.) in a full glass of water were given. This procedure in most cases eliminated the untoward gastrointestinal symptoms first noted. This dose was given only 3 times daily.

If, as recent work has shown, in endocrine dysfunction there is a disturbance of electrolyte balance and if allergy is based on an endocrine imbalance, then this might be a rational approach. The authors of this section feel that clinically we can demonstrate glandular hypofunction in a great many allergic individuals but we have never been able to demonstrate any disturbance of electrolyte metabolism in allergy following a great deal of work. An exhaustive laboratory study from the standpoint of salt and water balance in these individuals has been done

In the above report, striking benefit was noted in 29 cases of hay fever after the use of potassium chloride. This preparation was tried in other allergic diseases and it was found practically ineffectual in chronic asthma but, when

used along with a low salt diet, it seemed helpful. No toxic untoward effects were noted from the use of potassium salts.

Gastric distress was noted in a large percentage of our cases but this was decreased by giving a weak solution as recommended by Bloom. Most of our patients using potassium chloride had urticaria and in no case did we have a marked clinical improvement. We must always remember in treating allergic diseases, especially urticaria, that there are frequent remissions and exacerbations.

Harley³⁵ quotes D'Silva's discovery that the injection of epinephrine intramuscularly into animals is attended by a rise in serum potassium due to the liberation of potassium from the liver. He feels that it is possible that the beneficial effect of epinephrine in allergic individuals may be partially due to the potassium liberated

He employed the method of Bloom in which a 5-grain (1 Gm.) potassium chloride tablet dissolved in a glass of water was given a half hour before meals. He concluded that potassium chloride in the dosages employed failed to produce any significant degree of improvement in 43 allergic patients. The same results or results of no significance have been obtained in about 60 cases treated by the authors of this section. Dosages of 15 to 45 grains (1 to 3 Gm.) have been given daily

ENDOCRINE THERAPY IN ALLERGIC DISEASES

Many patients with allergic disease have associated with it some glandular dysfunction. We believe that many have some hypofunction of the adrenals, at least from their clinical symptoms. Truly allergic individuals are often asthenic,

fatigue easily, have a soft compressible pulse and a low blood pressure.

These patients often do well on adrenal extracts both by mouth and parenterally. H. B. Wilmer and M. M. Miller³⁶ have reported 13 per cent beneficial results in this type with intramuscular injections of cortical hormone processed by the Swingle-Pfiffner method. L. E. Prickman and G. A. Koelsche³⁷ treated a group of 19 patients with suprarenal cortical extract (cortin). Six of this group showed some slight symptomatic relief. These 6 had asthma. One patient had complete relief of his symptoms from treatments given 2 months apart. In all the rest, no relief was noted. These observers conclude that the intravenous administration of cortical hormone, suprarenal cortical extract (cortin) and supplemented by sodium chloride by mouth gives little or no benefit in a group of patients who had asthma and other allergic diseases.

Suprarenal extracts by mouth have also been used with varying success. We have treated a large group of cases with *suprarenal concentrate and gly-cortal*. The dosage of each is 4 to 8 capsules daily. These can be given with or without the addition of sodium chloride

These adrenal extracts, whether given by mouth or injection, do not have any marked specific effect in the symptomatology of allergic disease but they are adjuncts in treatment. They are to be used as supplementary therapy to the usual elimination and hyposensitization.

It is believed that they help reinforce the primary background of endocrine and nervous stability that is so often lacking in the allergic individual. At present, if an allergic patient manifests the clinical symptoms of hypoadrenia, it is well to supplement the usual therapeutic measures with a whole gland adrenal preparation

Endocrine therapy is often of extreme importance, especially in patients at the menopause. Preparations containing female sex hormones are often indicated in cases with complications associated with menses and the menopause. We have used progynon B and other estrogenic substances in doses varying from 500 to 2000 rat units at intervals of 4 to 5 days, beginning about a week after the last period and continuing until the next. After cessation of menstruation, the dose is given at the same interval, and the amount depends on continued indication or untoward symptoms developing.

Thyroid extract has proven a valuable adjunct in cases where there is clinical evidence of hypothyroidism or a low basal metabolic rate, or both A combination of thyroid extract and suprarenal concentrate has been highly efficacious in some of our cases.

This fundamental condition from which allergy inevitably results must be found before there is any marked advance in therapy. In the opposing action or synergistic functional activity of any one or a group of glands may be found the answer

Estrogenic substance³⁸ has proved an increasingly valuable supplement in therapy in patients who have allergic disease which has its onset during the menopause. To the present date, we have treated over 200 patients with estrogenic hormones and at times our results have been spectacular and produced beneficial results when all other modes of treatment had failed. We especially like to use it in menopausal urticarias and in cases of so-called neurodermatitis

HAY FEVER

Treatment — Specific hyposensitization in hay fever is accomplished in 3

different ways: Preseasonal; coseasonal and perennial. We also have recourse to rapid hyposensitization or the so-called "rush hyposensitization."

We can discuss the coseasonal procedure in a brief space. We commence pollen hyposensitization during the season only because the patient has failed to present himself for treatment before the onset of pollination. There are more chances of failure and the patient is more liable to a generalized reaction if treated entirely while he is absorbing pollen from the air. This disadvantage is eliminated to some degree by a routine we have followed in the past 2 years both in pollen asthmatics and in hay fever cases. Rapid hyposensitization is attempted and especially works well if the patient is placed in an air-conditioned pollen-free room.

In reviewing the literature from 1920 to the present, one finds that Besredka was the first to desensitize a patient via the rapid inoculation method. The title of his paper was "De Lavaccination Anti Anaphylactique" published in Compt. Soc de Biol. 1908, 65, 479.

In 1930 John Freeman published an article "Rush Inoculations" in the Lancet. His paper deals with the rapid hyposensitization with pollens in the treatment of hay fever and pollen asthma. The injections were given every 2 hours, starting with 80 units and reaching 20,000 within a period of 3 days. Of course, not all patients receive such high dosages. He believes that this method has its definite advantages in that it is not time consuming and that reactions can be prevented by careful observations during the 3-day hospital period

In 1937 Waldbott and Asher³⁹ published a paper entitled "Further Observations on Rapid Hyposensitization." This was a follow-up of an article published in the Journal of Allergy in 1934

by the same writers. Their conclusions were:

- 1. One is able to reach a high state of hyposensitization.
- 2 There is certainly some danger attached to this method.
 - 3 Late reactions occur more commonly.
- 4. The danger of reaction was lessened by the administration of several minute doses at the onset of treatment.

Nineteen cases of pollen asthma were treated in this manner. A complete course of pollen injections was given at intervals of 1 to 2 hours. The first dilution given was 1:10,000 and the first dose was $1\frac{1}{2}$ minims (01 cc). The maximum dose given was 7½ minims (0.5 cc) of a 1:500 dilution. Sixteen of the 19 cases were completely hyposensitized and remained so during the rest of the season Some have been put on perennial treatment while others we have allowed to go until the next season. One case became very toxic during the period of treatment and this procedure had to be discontinued. Two of the patients had no relief whatsoever. There were no more constitutional reactions encountered than we usually find in the preseasonal treatment. In only 1 case was it necessary to stop the injections.

The coseasonal procedure was attempted in 21 cases of hay fever during the last season; 8 were spring grass cases and 13 were sensitive to different fall weeds. Good results were obtained in 2 of the spring cases and 6 had complete relief. Two cases were treated in air-conditioned rooms. The spring season of 1938 was not a very bad one but at times symptoms were quite marked

Our results with the 13 fall cases were not as striking. The fall season in the Middle Atlantic States was one of the worst in several years. Four patients had complete relief; 7 had some relief, at least 50 per cent; and 2 patients had

no relief. Untortunately, only 2 of these patients were treated in air-conditioned, pollen-free rooms.

Precautions observed were:

- 1. If any local reaction was observed, the same dose was repeated or the interval lengthened to 2 hours.
- 2. The patient was entirely removed from contact with the offending substance.
- 3. Four of the patients were put in air-conditioned, allergen-free rooms.
- 4 Patients were hospitalized and kept in bed under constant supervision during the period of hyposensitization.
- 5 Injections should be stopped if any constitutional reactions develop.

A. Vander Veer⁴⁰ reports a study of the relative merits of the seasonal and perennial treatment of hay fever. At present, there is a great deal of controversy among allergists as to the better method. This article dealt with observations on an average of 430 patients annually. A questionnaire was sent to each patient who alone evaluated the results obtained. According to the chart published in the résumé, it was shown that the perennial results were uniformly better by 8 to 10 per cent than the seasonal This is according to statistics, but the human equation must be brought into the picture It is much easier to persuade a patient with complete relief to continue throughout the year than one who has been refractory to the seasonal injections. This factor may tend to place more of the satisfactory cases in the perennial.

There are 2 disadvantages in the perennial treatment. Many patients forget to take the injections and, if an interval of 5 weeks has elapsed, the risk of constitutional reaction is increased. There is always the possibility of a patient becoming saturated and into such a state that very small injections will give a constitutional reaction.

In general, the problem is best solved by choosing the right method for each patient, depending on temperament, sensitivity and previous results obtained. The preseasonal and coseasonal methods of treatment are quite necessary in many cases but, under ideal conditions and when there are no untoward symptoms, it is felt by a great many allergists that the perennial treatment is, by and large, the method of choice. Vander Veer considers that perennial treatment is more likely to produce a permanent so-called "cure" eventually than the other methods.

The maximum dosage in pollen treatment was the subject of a survey by Alexander.41 He found that the highest top dosage was 100,000 units or a 15 minim (1 cc.) dose of a 1:10 concentration. 42, 43 Several used a dosage as high as 2000 units only. The majority preferred maximum injections of 10,000 units. It is very interesting to note that about the same results are reported by men using such a variance in maximum dosage as shown above We feel that at least 5000 units should be attained but that better results are obtained if a maximum dose of 10.000 units or 15 minims (1 cc) of a 1.100 extract is reached

Care must be observed in starting patients. Vaughan⁴⁴ states that most hay fever individuals can be started on 10 to 20 units but in some cases a smaller initial dose is necessary. Each case of hay fever is individual in every respect and both local and constitutional reactions are less frequent if hay fever treatments are individualized and the tolerance of each patient carefully observed

Oral Ragweed Pollen Therapy.— Touart⁴⁵ in 1922 reported the results of oral pollen therapy in 6 patients. He started treatment 10 weeks before the onset of pollination. Some relief was obtained, especially in the early spring cases. He concluded that insufficient doses were given.

Also in 1922 Thommen⁴⁶ reported 90 to 95 per cent relief of hay fever in one patient and complete relief in another who had been given oral pollen treatment. Subsequent trial of this method did not justify its continued use.

Black⁴⁷ in 1927 and 1928 reported the results obtained from the use of ragweed preparations orally in ragweed sensitive patients. He found that a glycerin-saline extract of ragweed pollen could be used without any unpleasant effects except about 5 per cent had gastrointestinal disturbances. As has previously been demonstrated absorption from the alimentary tract was shown by finding the actual constituent of ragweed in the urine.

At this time Black felt that some results were obtained but not comparable with the hypodermic method. He abandoned the method because his results were not too satisfactory and inconclusive

During the ragweed season of 1938, Black⁴⁸ again used ragweed oral pollen therapy, using 40 patients and beginning treatment about a week before the onset of pollinosis. The initial dose was 500 units and he usually reached a maximum dose of 4000 units. Two patients experienced nausea and vomiting and the treatment was stopped. Eighteen obtained slight improvement and the effect in the rest was variable up to 4 who obtained excellent results.

Black concludes that oral pollen therapy gives satisfactory results in some cases but does not compare favorably with the results obtained by the hypodermic method

Stier and Hollister⁴⁹ in 1937 in a review of 383 cases stated that 79 per cent received over 50 per cent relief.

There is some doubt as to the absorption of pollen through the gastrointestinal tract in amounts that can be demonstrated. Black showed positive proof. Thommen also concluded that it was definitely absorbed. Bernstein and Feinberg⁵⁰ could not show that any amount was absorbed. Bernstein and Kirsner⁵¹ also reported that they could not demonstrate any absorption of ragweed pollen through the gastrointestinal tract.

Zeller⁵² in 1939, after a very careful study of 42 cases of ragweed hay fever on oral pollen therapy has drawn the following conclusions:

- 1. The absorption of ragweed pollen through the gastrointestinal tract could not be demonstrated by either direct skin testing or the passive transfer method
- 2. The group of patients studied does not support and show any apparent advantages in oral pollen treatment
- 3 The combination of oral and hypodermic pollen therapy has no advantages.
- 4 Untoward gastrointestinal symptoms such as discomfort, distention, nausea, vomiting and diarrhea were experienced by some patients, also malaise and exhaustion General reactions occurred in a higher percentage of patients using oral therapy than in those being treated by the hypodermic method

The consensus is that oral pollen therapy may help some cases but the percentage is very small In general, results have been very poor Local and general reactions were distressing at times, and we feel that there is no reason to use this form of treatment in preference to the hypodermic method of hyposensitization

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ARTHRITIS AND RHEUMATOID CONDITIONS

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Emotional and Environmental Factors—The possible importance of emotional and environmental factors in relation to remissions and exacerbations of rheumatoid diseases has been frequently intimated by individual experience. A study by Cobb, Bauer and Whiting has been conducted to determine how often there is a synchronism of social or emotional incidents and arthritic symptoms. A group of 50 patients with typical rheumatoid (atrophic) arthritis were examined in detail by a psychiatrist with respect to the social environment and adjustment The medical history, compiled by an internist, was entered upon charts recording the significant social and psychologic events in the subject's life In this way the correlation of time relationships between clinical and psychological episodes could be made evident

On this basis the series was divisible into 3 groups, viz, (1) those which show a close temporal relationship between life stress and arthritis, (2) those in which the relationship is doubtful, and (3) those in which no relationship is evident Thirty-one of the patients were found in the first group Financial worries, faniily, and marital difficulties were prominent among the precipitating factors Twelve were classified in the second group, showing doubtful relationship between arthritis and stress Only 7 patients presented no correlation. These

included the younger members of the series. A control group consisting of 25 patients with varicose ulcers was selected with comparable age and sex distribution. The social status of the study and control groups was the same. The procedure for analysis was identical. In only 3 of the control group was there any correlation between the onset of ulceration and social stress

On the basis of this comparison, it is concluded that environmental stress, particularly poverty, grief, and family worries bear more than a chance relation to the onset and exacerbation of atrophic arthritis. The therapeutic and prophylactic implications of this conclusion are obvious.

Etiology — The diagnosis of the 2 main groups of arthritis is at present based upon a classification depending chiefly upon pathological features. It is generally recognized that an etiologic classification is preferable masmuch as treatment based upon etiological factors might be made more effective. For these reasons it is proper to consider well conducted experimental studies bearing upon possible etiological agents From this point of view, several suggestive papers should be mentioned regarding newly described pathogenic agents producing experimental syndromes comparable to atrophic arthritis. Sabin has isolated 2 strains of a filterable pleuro-

pneumonialike microorganism from mice which possess specific tissue affinities. producing 2 characteristic syndromes in mice. Strain A multiplies in the brain, parietal and visceral peritoneum, pleura, and pericardium. It produces a specific exotoxin which has an affinity for the cerebellum. This toxin either kills the animals or leaves them with choreiform symptoms. The toxic substance may be produced in vitro, is thermolabile, and is neutralized by specific antitoxin. In addition to the neurological symptoms, it produces migratory polyarthritis in 40 per cent of animals. These symptoms disappear spontaneously in 4 to 6 weeks.

Strain B has a specific affinity for joints. It does not multiply in cutaneous, subcutaneous tissues or in the viscera or brain. This agent gives rise to chronic progressive proliferative ankylosing arthritis which resembles clinically and pathologically atrophic arthritis in man

Swift and Brown have cultivated pleuropneumonialike microorganisms from rheumatic exudates and from rheumatic nodules which exhibit the qualities of the pathogenic agent described by Sabin. The data offered are not sufficient to demonstrate the etiologic significance of these agents to rheumatic disease in man A more recent paper by Sabin brings further questions regarding the identity of this microorganism and the factor producing clinical arthritis in man by recording his inability to grow the agent from exudates obtained from 12 rheumatoid arthritics, from nodules of 3 patients, synovial tissues from 2, blood, pleural fluid, pericardial fluid, and heart muscle of 2 patients with rheumatic fever Previously obtained positive results apparently depended upon the use of mice which may act as carriers of the pleuropneumonialike microorganisms. Despite this uncertainty, a new experimental syndrome has been produced which may

provide valuable data applicable to the clinical problem.

An interesting series of observations has been conducted by Collier and associates on an experimental type of arthritis encountered in rats which pathologically resembles atrophic arthritis in man. Lesions appear in the joints of infected animals, whereas the visceral organs show no evidence of disease. No artificial cultures have been obtained but the disease may be transmitted from animal to animal by subcutaneous and intraperitoneal injection of exudates or of ground suspensions of tissue materials from infected animals. Transmission of the disease does not appear in animals caged together. Guinea pigs apparently are not susceptible to the disease. Rats which recover from the disease possess an immunity but fail to show the presence of circulating antibodies. organs of chronically infected as well as those of immune and hyperimmunized rats frequently contain the specific agent of rat polyarthritis. Blood apparently does not always contain the infective agent even in animals which bear the infectious agent in the organs.

Further illumination of the possible rôle of focal infection in arthritis is provided by experimental studies conducted by Cecil and Angevine on rabbits These animals developed arthritis in response to the intravenous injection of hemolytic streptococci in a frequency of 85 per cent. Single and multiple foci of infection were produced in rabbits by injecting suspensions of these organisms into the gums, sinuses, prostate, testes, eye, pleural and peritoneal cavities, joints and skin. Segments of the fallopian tubes, renal pelves, gall-bladder were also injected. Viable streptococci were fed in large doses for prolonged periods Cotton plugs containing the microorganism were packed in the nares. In most in-

stances the sites of application were sterile after a short period of time. Arthritis developed in only 11 of 100 rabbits, all of which showed positive blood cultures shortly after injection. Arthritis appeared most frequently in animals receiving injections into the gums, sinuses and male genitalia. The foregoing data indicate the necessity for consideration of host susceptibility as well as the site of entry. Repeated inoculation apparently produced no more arthritis than a single dose in susceptible animals.

A further and more detailed experimental study on infection as an etiological factor in arthritis is reported by Cecil, Angevine and Rothbard. Intravenous injections of both Streptococcus hemolyticus and viridans produced an arthritis with high frequency. Injection of Staphylococcus aureus, pneumococcus and B paratyphosus A produced a similar arthritis but with lesser frequency. Articular lesions were produced more frequently in females than in males The disease was apparently produced during the stage of bacteremia. This experimental syndrome was associated with an increase in sedimentation rate in 97 per cent, an elevation of agglutinin titers in 89 per cent and positive skin reactions with streptococcal filtrates in 42 per cent The synovial lesions were comparable to those in atrophic arthritis in man

While similar observations have been reported previously, the foregoing data emphasize the potential importance of transient bacteremia arising from a septic focus

Pathology — A contribution to the pathology of atrophic (rheumatoid) arthritis and of rheumatic fever is made by Fisher. Many of the previously reported observations on the pathological changes in the joints of arthritics have been made upon tissues obtained during the late and often quiescent periods of the dis-

ease. The data reported by Fisher have been obtained from clinically active patients subjected to arthrotomy. operation, followed by lavage with an antiseptic solution (Dakin's solution) is regarded as of considerable therapeutic value in certain acute cases of the atrophic type. It is recommended particularly when large superficial joints such as the knee are affected. In certain subacute cases partial synovectomy has been carried out. These measures may lead to reduction in acute symptoms. In some refractory cases a marked lowering of the sedimentation rate has followed the operation. This suggests that the pathological processes in joint tissue per se may be directly responsible for the elevation of the sedimentation rate of the erythrocytes of the blood.

According to Fisher the synovial tissues from atrophic arthritic patients are strikingly similar to those from patients with rheumatic fever. Giant cells of the Aschoff type appear in both In addition to this common feature both show areas of fibrinoid degeneration. In the light of the similarity of pathological patterns in these 2 conditions Fisher regards the 2 clinical conditions as manifestations of the same fundamental pathological proc-This hypothesis is not fully validated, however, since there is some question in the minds of certain competent students as to the pathological identity of the subcutaneous nodules present in both conditions. Emphasis is placed upon the cultural sterility of these lesions. Furthermore, the tissue reactions are markedly different from those produced by known infectious agents such as the streptococcus and staphylococcus in situ

The somewhat widely held view that rheumatic fever and atrophic arthritis are similar pathological entities is questioned by Collins. Acute rheumatism

shows a basic pattern of elementary tissue changes, consisting of exudation, mesenchymal proliferation, connective tissue degeneration and leukocytic infiltration. While these same phenomena occur in atrophic arthritis, the distribution of the lesions consequent upon these processes is conspicuously different in the subject with rheumatic fever and the subject with atrophic arthritis. Fibrinoid degeneration, consisting of swelling of collagen, or bundles of fibrinous tissue with exudation into tissue spaces gives rise to a granular focus of necrosis. According to Collins this change is preceded or followed by proliferation of mesenchymal cells and invasion by leukocytes.

The specificity of the fibrinoid change is doubted in view of the fact that a similar lesson appears in association with the Arthus phenomenon and other conditions associated with tissue hypersensitivity. Comparable lesions may also appear in response to the local presence of irritants or as a result of vitamin C deficiency A similar lesion appears in granuloma annulare which is clinically unrelated to rheumatic lesions. Thus it is evident that the general histological similarity of subcutaneous nodules of rheumatic fever and of atrophic arthritis does not require the conclusion that they are of like origin. Further evidence of dissimilarity between the pathologic features of rheumatic fever and atrophic arthritis is indicated by the localization of vascular lesions in the joints of the latter as compared with generalized polyarthritis in the former.

Additional pathological differences are pointed out in reference to the articular lesions. In rheumatic fever the synovial tissue shows edema, congestion, slight leukocyte invasion with occasional foci of proliferated large mesenchymal cells. In atrophic arthritis the inflammatory proliferation of synovial tissue is more

marked, and characterized by growth of large foci of lymphocytes or plasma cells. In view of the fact that the latter changes are seen in traumatic tenosynovitis it appears that the response is general and not a specific one. Furthermore, a variety of specific infections, Malta fever, tuberculosis, gonorrhea, may produce lesions of polyarthritis which require more than superficial inspection for differentiation.

The fact that most studies show that the joint tissues are sterile by examination with usual culture media may not exclude the possibility that the lesions are irritated by the actual presence of microorganisms according to Collins. He considers the evidence of metastatic infection from focal sites of entry as too well founded in clinical experience to exclude the possibility on the basis of negative laboratory data alone. By the same token, caution is advised regarding the interpretation of experimental data bearing upon etiology. The final proof that an experimental symptom complex is analogous to rheumatic disease depends not alone upon similarity of connective tissue changes but upon an identity in all objective pathological and clinical features

Osteoarthritis

A comprehensive survey of osteoarthritis (hypertrophic) is presented in a Heberden Lecture by E. Fletcher (1939). The standards suggested for diagnosis of hypertrophic arthritis include clinical and roentgenographic criteria, both of which are regarded as essential for proper evaluation. The presence of pain must be established as directly referable to the joint and not referable to periarticular tissues or other sites. By the same token, swelling must be established as articular in nature and may be due either to increased volume

of joint fluid or to enlargement of synovial or bony structures. Localized joint tenderness is regarded as an index of clinical activity. While crepitus is a fairly useful index of tendinous inflammation it is of doubtful significance in respect to pathological activity within the articular structure. Similarly, limitation of motion is chiefly useful as evidence of past damage. One exception occurs in the shoulder joint wherein limitation of motion may provide an important and sometimes the only measure of clinical activity. Deformity, muscle wasting and stiffness may be present even in joints which show no active lesion. Except for these limitations which are often overlooked, the aforementioned clinical features are essential in evaluating the clinical activity in a case of hypertrophic arthritis.

The roentgenographic features must be critically considered. The positive diagnosis of hypertrophic arthritis depends upon differentiation from a variety of conditions, particularly from the infective type of arthritis. In this respect hypertrophic arthritics show no loss of joint space and exhibit dense thickening in the form of bands rather than mixed areas of opaque and translucent areas in the line of cartilage. When sclerosis is present it is usually not very dense There is no blurring of cancellous bone but there are outgrowths at the junction of cartilage and synovial membrane Finally, the joints may contain loose bodies, although this is not a constant feature.

Symptoms—In a series of 103 cases satisfying the aforementioned criteria 2 associated clinical symptoms appeared with notable frequency, viz, obesity and high blood pressure. The relative frequency of hypertension and obesity in hypertrophics is indicated by the fact that while only 108 per cent of persons

in a large sick population show hypertension, 43.7 per cent of hypertrophic arthritics present this symptom. Obesity is encountered in 6.2 per cent of sick persons in an average cross section of the population, whereas 49.5 per cent of hypertrophic arthritics present this feature. In the light of these comparative statistics Fletcher regards obesity, hypertension and hypertrophic arthritis as a triad of symptoms. The pathogenesis of hypertrophic arthritis should be illuminated by considerations embracing both obesity and hypertension. Emphasis 1s placed upon several conditioning factors which modify exogenous obesity. While arising primarily from excessive amounts of foodstuffs, the consequences of this type of obesity are not explained by a simple statement of a positive caloric Secondary physiological conbalance. sequences follow the deposition of fat which are far beyond those arising from the mechanical effects of excessive weight alone. Many observers have regarded overeating with consequent overweight as a factor contributory to arthritis through micro-traumata alone.

The view that hypertrophic arthritis is due to the wear and tear of repeated traumata and cannot be cured because articular cartilage cannot be rejuvenated is regarded as untenable. Statistics collected by Fletcher and others show that this is contrary to clinical experience Cases of hypertrophic arthritis are often rendered symptom free Furthermore, some cases appear early in life when wear and tear can scarcely be a determining factor.

It is widely appreciated that there is no clear parallelism between the extent of pathological change and pain. Many joints showing marked evidence of overgrowth by x-rays show slight degrees of pain. The view is advanced that the symptoms of hypertrophic arthritis are

superimposed upon degenerative qualities which mark older age. The acute flare-ups are regarded as inflammatory episodes arising from infectious factors or from the aseptic injury produced by movement. This view is in harmony with the fact that osteoarthritic pathology may be superimposed upon an arthritis of known infectious origin. Traumatic factors alone are likewise able to produce lesions comparable to those seen in hypertrophic arthritis.

The origin of the pain associated with hypertrophic arthritis is not identical in all instances. It may arise from elevation of the periosteum by proliferation of marginal tissue and by pinching of synovial villi. Pain tends to disappear with the development of calcification. It may also appear as a result of exposure of subchondral bone and by muscle spasm associated with fibrosis Pain may be referred to knees by lesions in the hip.

It is possible that interference with the lumbosacral nerves may produce hypertrophic arthritis in the hip joint. Fletcher suggests that the pathogenesis of hypertrophic arthritis is not determined by the avascularity of cartilage alone but is conditioned by many factors including the enervation of the joint structures. The influence of endocrinous factors is also regarded as important, particularly in cases with associated obesity and hypertension. The association of hypertrophic arthritis in 15 per cent of 103 cases at the menopause is noted It is suggested that so-called menopausal arthritis is pathologically described as hypertrophic synovitis. Toxemia may play an important rôle both by direct action upon the articular structures and indirectly through action upon the endocrines. It is concluded that adequate therapeutic programs must include measures capable of affecting a wide variety of deviations.

Treatment and Prophylaxis — The problem of treatment and prophylaxis requires consideration of the rôle of age in arthritis. According to a number of students, the factor of age is particularly important in relation to hypertrophic arthritis. Inasmuch as lesions in the cartilage are found with increasing frequency and magnitude with advancing years, it is concluded that hypertrophic arthritis is an invariable result of old The corollary is advanced that hypertrophic arthritis is not open to therapy, and nothing need be done about This nihilistic view is biologically narrow. The fact that hypertrophic arthritis appears most frequently in the latter decades of life makes it important to consider the clinical picture of the disease against the background of the age group to which these patients belong.

The observations of Todd on the phys-10logical ageing of the skeleton and locomotor systems represent a serious attempt to state the problem in broad biological terms. The similarity of certain clinical features to those characterizing advancing age is recognized However, it is maintained that normal processes of ageing are regular, whereas those of disease are disorderly. The diminution in the water content of cartilage and the atrophy of joint margins are regarded as orderly processes compatible with ageing. However, the fusion of the vertebral joints and fusion of the sacroiliac are regarded as expressions of frank pathology in no way related to ageing processes

It is observed that osteoporosis, indistinguishable from the halisteresis of advanced years, is frequently present in persons of mature and youthful age, suffering from chronically impaired constitutional health. It is further noted that the bone pattern in old age is suggestively similar to that produced by

vitamin C deficiency. Changes of joints with age are like those of cartilage and bone. The synovial membrane shows no primary alteration with age. However, it may undergo modification in ioints wherein cartilaginous changes are In these instances there are thickening of the capsule; papillary projections into the joint space and collections of lymphocytes around the blood vessels. The cartilaginous changes consist of fibrillation, degeneration and destruction. Associated with this the subarticular bone is thickened, the marrow spaces become filled with fibrous tissue. Cysts also appear. Exostoses, lipping, further contribute to the picture of hypertrophic arthritis. It would appear that while there may be conditions favorable to the development of hypertrophic arthritis with advancing years, this factor alone does not explain hypertrophic arthritis. Todd states that it is the accumulation of injuries with increasing years, followed by imperfect repair, which results in the lesion in the body of the aged. The therapeutic corollary to be drawn from this is that the hypertrophic arthritic should be properly protected from apparent injurious factors just as well as the atrophic arthritic

Menopause Arthralgia

F. C Hall describes a group of 71 cases marked by joint symptoms which developed at the time of artificial menopause. These subjects presented a symptom complex which has long been considered by many as a clinical entity, described variously as climacteric arthritis, menopausal arthritis and as menopausal arthralgia. The frequency of this syndrome varies in the experience of different observers. It apparently escapes notice by many gynecologists and endocrinologists. On the other hand, one study of 1000 women at the meno-

pause revealed evidence of rheumatic pains, arthritis, or fibrositis in 237. In addition, the frequent relation of factors involved in the menstrual cycle to the ebb and flow of symptoms of arthritis in women is suggestive evidence of the importance of ovarian or other endocrine function in the symptoms which develop at the time of the menopause. The well-known favorable influence of pregnancy in some types of arthritis and the exacerbation which may occur after term indicate a positive correlation between gonadal function and certain symptoms. Castration may be followed in some instances by symptoms of joint, bone, and muscle pain simulating that associated with chronic arthritis. Further evidence of the rôle of menopausal factors in certain cases of arthritis is provided by the favorable influence of endocrine factors on the course of the disease. One class with lowered basal metabolic rates are benefited by thyroid medication. Another class not showing myxedematous features are made worse by thyroid therapy.

Symptoms—The symptoms presented by patients with arthritis at the menopause are variable. Many of them have their origin in vasomotor disturbances. One conspicuous feature often present is a chronic hypertrophic synovitis. Neuralgia is also often present.

The series of patients studied by Hall included 71 women whose chief complaint was an arthritis following removal or destruction of the ovaries. Fifty-three had arthralgia which developed from 1 to 10 weeks after panhysterectomy. This prominent symptom was associated with various combinations of other menopausal features, viz, hot flashes, sweats, insomnia, exhaustion, dizziness, headache, parathesias, emotional instability, and gastrointestinal disturbances. The joints showed slight, if any, change by x-ray

examination. Tenderness was absent. The sedimentation rate was generally normal or slightly elevated. Thyroid medication increased the symptoms.

Treatment - Relief from joint pain and other symptoms was achieved by adequate doses of estrogenic substances. Progynon, the benzoic acid ester of dehydrofollicular hormone, estradiol, dissolved in sesame oil was administered intramuscularly, in doses of 10,000 international units twice weekly, for a period of 4 to 6 weeks. Improvement was usually noted only after the third week and occasionally after the sixth week of therapy. The first signs of improvement included better sleeping, greater endurance, fewer flashes, and sweats, diminution of gastrointestinal symptoms and, finally, decreased joint pain and stiffness. Overdosage is evident by sore breasts, pelvic congestion, leukorrhea, and malaise. Inadequate dosage resulted in therapeutic failure. Of the 53 patients in the arthralgic class. 40 received what was considered an adequate dosage, 80 per cent were helped and 70 per cent responded in a striking and dramatic manner

The second group of patients in this series of castrates exhibited unquestionable evidence of true arthritis, showing atrophic, hypertrophic, or mixed pathological lesions All of these were well until castration In view of the absence of any other evident etiological factor, it would appear that the removal of internal secretions from the ovaries constitutes a direct or indirect cause of certain cases of true arthritis However, this conclusion is not fully warranted upon the basis of the data available and it is stated that only 50 per cent of this group responded favorably to estrogenic therapy The menopausal symptoms and the arthralgia were relieved, the general state of the patients was improved and it appeared that even the arthritis was improved by this endocrine therapy. These observations justify the application of estrogenic treatment to patients with symptoms of arthralgia and suggest the desirability of extending this measure to certain patients with true arthritis appearing at the time of the menopause.

Lymphogranuloma Venerea and Arthritis

The association of arthritis consisting of a rather well-defined pattern of symptoms with lymphogranuloma venerea in 24 patients has been observed by Dawson and Boots. Whether this constitutes a distinctive clinical syndrome is regarded as open to question but is nevertheless considered of practical importance. The cases presented positive Frei reactions and most of the subjects showed other evidence of infection with lymphogranuloma venerea The synovial fluids when cultured in the usual manner were sterile. The joint fluids were variable in quantity and general appearance. these respects the fluids presented no characteristic qualities The clinical features were somewhat more constant, showing generally a chronic, indolent course marked by a tendency to relapse. Intermittent hydrops with occasional acutely tender, painful joints was observed While polyarticular involvement was frequently present, there was a definitely high frequency of lesions in the knees, ankles, and wrists. In contrast to the true arthritides, the apparently serious lesions were seen to persist for weeks or months without evidence of destruction of the articular cartilage or bone in these cases Roentgenographic examination revealed only periarticular swelling with effusion into the joint spaces. Dawson observed that intravenous administration of Frei antigen appeared to exert a favorable influence on the course of some cases under observation but was

unable to state which form, antigenic or chemotherapeutic, is more effective in the treatment of this condition.

Pilot calls attention to the association of erythema nodosum with lymphogranuloma venereum, citing a case in which a typical lesion was produced by Frei antigen. The rather frequent appearance of erythema nodosum with rheumatic diseases of unknown etiology adds further cogency to the consideration of lymphogranuloma venerea as a possible etiological factor. However, it should be observed that reactivity toward the Frei antigen may remain even after the complete healing of the primary lesions so that a positive Frei reaction cannot alone incriminate the lymphogranuloma as the immediate etiological factor in all arthritics who present positive reactions. The association of this general clinical pattern with lymphogranuloma venerea apparently is not rare, being noted also by Ramey and by McEwen (1939) Ramey observed that exacerbation of the articular manifestations in cases appeared during activity of the colonic and rectal lesions Furthermore, the latter lesions were apparently controlled by antimony and potassium tartrate administered intravenously. The rheumatoid symptoms in these patients were also diminished after the same therapy Sulfanilamide likewise afforded at least temporary relief from both colonic and articular symptoms.

Allergy and Rheumatism

The possible rôle of allergy in rheumatism has been approached from many angles. A study by Traut provides a partial answer to the question as to the rôle of the hypersensitive state in the arthritic. While the thesis is not held that arthritis is primarily an allergic disease, the idea is suggested that certain allergic symptoms and arthritis tend to occur in

a class of labile individuals. In the present series, 175 patients with atrophic arthritis, 129 patients with hypertrophic arthritis. 55 patients with rheumatic heart disease and 100 controls selected from a general sick population were surveyed with respect to associated symptoms of asthma, hay fever, urticaria, The atrophics showed these symptoms in 18.8 per cent, hypertrophics in 302 per cent, rheumatic heart cases in 309 per cent, and the controls in 19 per cent. When rhinitis and migraine which frequently have an allergic basis were included, the atrophics presented association in 54.1 per cent, the hypertrophics in 612 per cent, and the controls in 37 per cent. When the degree as well as the kind of hypersensitivity is considered, the rheumatic groups show from 2 to 3 times as much allergy as do the controls.

In addition to the higher frequency of allergic manifestations among arthritics, the rheumatic patient reacts to bacterial invasion and climatic changes in a manner different from the normal subject. Surgery involving focal infection often aggravates the symptoms of the arthritic whereas these measures normally provoke but slight reaction among other groups of individuals This situation. whatever may be the nature of the underlying mechanism, bears an important therapeutic corollary, vis, that the arthritic subject should be handled conservatively with respect to factors which may disturb his unstable physiological equilibrium

Aspiration of Joint Fluids

Aspiration of joint fluids is recommended as a safe and useful procedure by Kling. Comparatively simple examination of joint fluid provides many significant data. The technic for obtaining synovial fluid is variable, depending upon

the joint examined. The site of aspiration is cleaned with soap and water, painted with iodine and then rinsed with alcohol. The site may be conveniently anesthetized by injection of 2 per cent novocain. After the anesthetic has taken effect, the skin is pulled aside over the site of aspiration in order that the deeper structures may be covered by intact skin, following the removal of the needle. A Luer syringe fitted with a 15 or 16 gauge needle is used to withdraw the The needle should be provided with a short bevel and care should be exercised to prevent injury to the articular surface. Pressure by hand helps to empty the fluid from the joint. If blood enters the syringe during aspiration, the needle should be withdrawn. While other joints may be subjected to study, the fluid of the knee is most frequently ex-For the sake of a maximum degree of safety, the suprapatellar bursa is recommended. The needle is inserted about 2 inches above the patella on the side which shows the largest amount of bulging. When necessary, the popliteal pouch is aspirated by insertion of the needle about 2 centimeters to either side of the midline, extending obliquely forward and outward to avoid the popliteal vessels.

Measures, such as injection with air or with opaque dyes for visualization by x-rays and inspection of joint cavities by the arthroscope, are regarded as valuable for specialized studies but are considered as unsuitable for general use.

The data obtainable by examination of synovial fluid include the following diagnostically important features. In contrast to the normal negative pressure, very high pressures are encountered, particularly with acute effusion Lesser volumes and pressures characterize chronic effusions. The normal clear transparent fluid is changed to one of opaque appear-

ance if the fluid is infected. The cell count is raised from a normal range of 200 to 450 per cubic millimeter to levels as high as 10,000 in infected fluids or in mild chronic lesions. Total cell counts in excess of 10,000 per cubic millimeter indicate an acute severe lesion. Bloody fluids are indicative of hemorrhage into the joint space suggesting either traumatic lesions, hemophiliac or scorbutic processes. The most conspicuous quality of synovial fluid. viz., the viscosity, is chiefly due to the presence of mucin. The relative viscosity ranges from 10 to 20 times that of water. In certain chronic lesions, the viscosity relative to water may be as high as 108. In acute cases and in fluids of a transudative nature, the viscosity may be much lower, e.g., 1.6, even less than that of normal blood serum transudates, the relative viscosity may be less than 10, whereas the viscosity of effusion is usually greater than 10.

Variations from the normal specific gravity bear the same interpretation. A fluid with a specific gravity of 1003 is indicative of a transudative process, and a fluid with specific gravity of 1.03 may be indicative of an exudative process. Simple chemical examination is also useful The presence of considerable amounts of fat is indicative of traumatic injury to the fat pads A bilirubin level in excess of 5 indicates a traumatic or hemorrhagic lesion, whereas a value of less than 5 indicates an inflammatory process. Uric acid is often high in gouty joints Calcium may be low in hypertrophic lesions Sugar is uniformly low in infected fluids. Mucin is low in atrophic arthritic fluids and in frank infection

The acid base balance of normal fluids is usually poised at a level somewhat higher than blood. In contrast, infected fluids often show a pH less than 7.3. This is partly due to the excessive production

of acid metabolites by both the invading microorganism and by the leukocytes.

Kling considers the comparative sedimentation rate of erythrocytes in synovial fluid and plasma as useful in evaluating the severity of the process in a joint. The comparative rate in the affected joint is high. The differential count is additionally valuable. The presence of more than 10 per cent of synovial cells is indicative of synovitis. Neutrophils predominate in acute and active processes, while high lymphocytic and monocytic counts are suggestive of more chronic processes.

Septic joints can be further identified by cultural methods Positive cultures may be obtained in frankly purulent joints, of streptococci, staphylococci, or pneumococci. Gonococci can be positively cultured in from 10 to 64 per cent of the cases otherwise identified Chronic infective processes usually yield negative results on culture Smears may reveal Mycobacterium tuberculosis and gonococci Animal inoculation is the procedure of choice in the examination for tubercle-forming agents. Synovial fluids share with sera the qualities of yielding positive Wassermann reaction in syphilis and positive complement fixation in about 80 per cent of the cases of gonorrhea

Histological examination of loose bodies is an aid in identifying their origin Synovial tissue fragments, fibrin rice bodies, and cartilage segments can be easily recognized

Gout

Diagnosis—The diagnosis of gout is apparently being made with increased frequency Important features to be considered in the diagnosis and treatment of gouty arthritis are described by Lockie Gouty arthritis is to be considered as a possible diagnosis in males

who show recurrent attacks of arthritis. This condition is more frequent in males after the age of 25 years than before. Identification of sodium urate in tophi is pathognomonic. Elevation of the level of uric acid above 5 mg. per 100 ml. is often present in the gouty subject, but is insufficient alone to provide a certain basis for diagnosis. Roentgenograms are useful, particularly in the later stages of the disease but the characteristic features may be lacking in the earlier stages. In view of these somewhat uncertain features, provocative and therapeutic tests assume an important place in differential diagnosis.

Treatment — The group of patients observed by Lockie consisted of 75 with gouty arthritis and 50 with other forms of arthritis The response of the gouty arthritics to colchicine was uniform, all experiencing marked relief of symptoms. The drug was administered in divided doses over a period of 24 to 72 hours until the patient had diarrhea. sometimes occurred after a few doses of 1'69 grain (1 mg) The pain disappeared first, followed in a few days by disappearance of aching in the joints The relief induced by colchicine was greater and longer than that induced by emchophen or by salicylates

Contrasting with this response, the nongouty arthritics experienced only mild and transient relief, if any, with a return to the original pretherapeutic discomfort following the same dose of colchicine Both hypertrophic and atrophic arthritics were included in this group which failed to show response to colchicine.

The provocative test, consisting of the feeding of a diet low in carbohydrate (50 Gm), low in purine and high in fat (220 Gm.), described by Lockie in earlier communications has been applied to patients with a positive diagnosis of gout at a time be-

tween expected attacks. In 9 of 10 experiments a typical acute attack of gouty arthritis was induced. This type of diet apparently does not aggravate the symptoms in patients suffering from other kinds of rheumatoid diseases.

The practical implication of these measures is obvious. The test with colchicine is a convenient procedure, easily applied and serves a double purpose, viz., therapeutic and diagnostic. The provocative test may serve a useful purpose in demonstrating the presence of gouty arthritis and further demonstrates the desirability of maintaining known gouty subjects on a relatively low fat diet.

Therapy of Arthritis

Gold Therapy — The use of gold salts in the treatment of patients with arthritis is apparently gaining in favor among physicians, if the number of papers dealing with this subject provides an adequate index. While some investigators are enthusiastic regarding this drug, others emphasize its limitations and advise caution in its application. A progress report by Snyder, Trayer and Kelly on 100 cases of arthritis treated with gold sodium thiosulfate and aurocein provides a representative appraisal of these drugs. In this series only patients who had proved to be refractory to all other accepted methods of treatment were included Furthermore, patients with evidence of hypersensitivity or with histories of cutaneous, hepatic, renal, or gastrointestinal irritability were excluded Data were obtained on the cell count and sedimentation rate of the blood, the urine composition, before and during the course of therapy. Aurocein, a 5 per cent solution of sulfhydryl gold naphyl tri-sulfo-carbonium derivative was administered intravenously twice weekly for a period of 12 weeks Intervals of 6 weeks divided series of injections. Injections were discontinued when toxic reactions appeared and were not continued until symptoms disappeared. Gold sodium thiosulfate in distilled water was administered intravenously in variable doses starting at ½ grain (5 mg.) with a stepwise increase to 1% grains (100 mg.) during 7 injections and continuing with 1% grains (100 mg.) doses until 900 to 1000 mg. of the salt had been given. This quantity was given during a period of from 6 to 8 weeks.

The patients under observation included 50 atrophics, 20 hypertrophics and 30 patients with mixed arthritis. Brilliantly favorable results apparently did not appear, but 48 per cent of the atrophics, 45 per cent of the hypertrophics and 26 per cent of the mixed cases showed some degree of clinical improvement during the course of therapy. Improvement was encountered more frequently in patients who had the disease for short periods and less frequently in patients who had the disease for more than 2 years. Contrary to results recorded by other observers, the frequency of improvement was not less but greater for the patients over 40 years of age than for those of 20 to 40 years of age. There was a lack of correspondence between the general clinical improvement and the sedimentation rate. An increased rate was noted in 47 per cent of the patients classified in the improved group

Toxic reactions were present in 17 patients. These consisted chiefly of dermatological lesions, most of which consisted of rashes lasting no longer than a week. In 1 instance the lesions persisted for 2½ months. Gastrointestinal symptoms appeared in 4 cases. Marked edema of the glottis developed in 1 patient who had to be relieved by tracheotomy. No fatalities occurred in this series. Toxic reactions sometimes ap-

peared even when small doses were administered.

In the light of these studies it is concluded that gold salt therapy is too dangerous for general use. This form of therapy should be employed only when the case has been shown to be refractory to more conservative measures.

Key, Rosenfeld and Ljoflat record experience with the use of myochrisine (sodium aurothiomalate) in 53 patients with classical atrophic arthritis, 2 patients with rheumatic fever, 4 patients with gonorrheal arthritis, 9 patients with spondylitis, ankylopoietica and 2 patients with lymphogranuloma. These patients had previously been subjected to various therapeutic procedures without arresting the pathological processes. The previous unsatisfactory states of the patients were regarded as constituting adequate controls. A dose of $\frac{3}{4}$ to $\frac{1}{2}$ grains (0.05 to 0.10 Gm) was administered weekly until 30 grains (2 Gm) of myochrisine had been given. Rest periods of 6 weeks were allowed. Patients with secondary anemia were given liver or stomach extracts (lextron or reticulogen). Patients with anorexia and constipation were provided with liberal accessory supplies of vitamin B Patients with bone atrophy were provided with calcium and cod-liver or haliver oils. Patients showing decreased capacity to remove glucose from the blood were given a low fat, high carbohydrate diet with added vitamin B

If the patients were overweight, they were reduced by submaintenance supplies of Calories, if underweight, they were provided a liberal quantity of Calories Toxic reactions from gold therapy were relatively mild on this regimen. In a few patients who developed mild skin reaction or irritations of the mucous membranes, the administration of *nicotinic* acid in doses of $2\frac{1}{4}$ to $4\frac{1}{2}$ grains (150)

to 300 mg.) daily was beneficial. The relief of toxic symptoms was usually prompt under this measure. Toxic reactions appeared in 44 of the 70 patients. These were comparable to those previously described. Care and vigilance is advised in recognizing the early symptoms of toxicity. In none of the classes except the atrophics was the result of gold therapy remarkable. In 2 the arthritis was aggravated, 6 no improvement, 7 improved but were not accessible for final checking, 4 slight improvement, 13 moderate improvement, 18 marked improvement and in 3 complete arrest. In the opinion of the investigators, the basal regimen did not account for the clinical improvement seen in these patients.

Sulfur Therapy—The indications for the use of sulfur and its compounds in the treatment of arthritis have been reviewed by Comroe. For many years sulfur has been administered to countless arthritics upon empiric grounds, orally, parenterally, and transcutaneously with baths, ointments The recent exploitation of sulfur products has been based upon a supposed defect of the metabolism of sulfur in the arthritic subject been noted that an abnormally low content of cystine in the fingernails is frequently encountered among patients with arthritis This has stimulated the use of sulfur in the treatment of arthritis. Elaborate hypotheses have been erected upon this fact, indicating an increased requirement, decreased intestinal absorption, increased destruction or disturbed assimilation of sulfur

While significant pharmacological effects may be produced by sulfur and sulfur compounds, many observers report conflicting data regarding sulfur metabolism in arthritis. The Council on Pharmacy and Chemistry of the American Medical Association has considered colloidal sulfur preparations as unacceptable

for the treatment of arthritis in the light of present information.

Comroe cites his own observations showing that the cystine content of nails varies widely among normals and nonarthritic controls. Low values are encountered in subjects with atrophic arthritis; similar values were present in patients with chronic illness of various kinds. Normal values were also found in patients with atrophic arthritis. On the other hand, lowered levels of cystine were present in elderly persons with and without hypertrophic arthritis. Furthermore, patients apparently benefited by measures including sulfur therapy failed to show increments in the cystine content of the nails.

Data from a therapeutic study of colloidal sulfur in 30 patients with atrophic arthritis and in 30 patients with hypertrophic arthritis are also presented. These patients were carefully selected, and each one was observed for a period of 3 years Colloidal sulfur was administered daily or biweekly by the intravenous route, beginning with 1'60 grain (1 mg), doubling the dose with each succeeding injection until a dose of ½ grain (30 mg.) was injected. A total of 5 grains (300 mg) was not exceeded in any series. Rest periods of 10 weeks were allowed between courses of injections. Intramuscular administration was conducted with doses from 160 to 13 grain (1 to 20 mg) biweekly until a maximum of 5 grains (300 mg) were given

Comroe concludes that the results of sulfur therapy are no better than, and in many instances not as good as, those obtained by general measures including rest, physiotherapy, removal of focal infections. In view of these considerations, sulfur treatment is not recommended as a routine procedure. If improvement is not evident under conservative therapy cautious administration of sulfur may be

indicated. Inasmuch as such refractive cases are limited in number, the field of application for sulfur treatment in arthritis is narrow.

An important contribution bearing upon sulfur metabolism and the effect of sulfur administration in rheumatoid arthritis has been made by Freyberg, Block and Fromer. These investigators planned their studies to answer 2 practical questions, viz., whether there is a fundamental abnormality in sulfur metabolism in the patient with rheumatoid (atrophic) arthritis, and whether the administration of sulfur has a beneficial influence on sulfur metabolism in the atrophic arthritic. Both of these questions have been raised many times and variously answered. Since these studies were conducted under precisely controlled conditions, considerable weight is to be attached to the data obtained.

Both atrophic arthritics and normal subjects were placed upon identical regimens, including the ingestion of constant diets, low in sulfur. Distilled water was allowed ad lib. After adjustment of the subjects to the regimen had been established, quantitative collections of urine were made and analyzed for nitrogen, sulfur, together with the fractional distribution of compounds of the latter. The values so obtained were considered as controls for comparison with those obtained after the administration of colloidal sulfur intravenously, intramuscularly and orally, and after sodium thiosulfate orally. In addition to these data, the cystine content of fingernails was determined at appropriate intervals. The capacity of the subjects for detoxifying substances like indole by conjugation was estimated by the determination of urmary ethereal sulfate following the oral administration of thymol. This functional test was conducted before and during the administration of sulfur. In this way it was as-

sumed that any enhancement of the capacity to dispose of toxic substances conferred by sulfur would be made evident by an increased output of the sulfur derivative of thymol.

These data revealed no significant difference in the way in which sulfur and its compounds are eliminated by normal and by arthritic subjects. The metabolic effect of sulfur administration was the same for both classes of subjects. The surprising fact was revealed that the total amount of sulfur eliminated following sulfur administration exceeded the quantity administered. In the light of this, it is evident that the administration of colloidal sulfur cannot be expected to prevent or diminish a deficiency of sulfur when such a deficit exists. Furthermore, injected sulfur appeared as inorganic sulfate and hence cannot be expected to confer an increase in the capacity for detoxification of toxic substances

There were no demonstrable differences in the capacity of arthritics to conjugate thymol with sulfuric acid as compared with this function in normal subjects Sulfur medication was not followed by an increase in the cystine contents of the fingernails. In the light of their data, these investigators conclude that there is no evidence of an abnormality or deficiency in sulfur metabolism in atrophic arthritis These conclusions are in essential agreement with those reached by other workers in this field If there is any beneficial effect of sulfur therapy in arthritis it must apply to a limited number and act in some unknown way which is not made evident by the biochemical methods now available

Vitamin Therapy—The use of vitamin D in large doses (200,000 to 1,000,000 units daily) has been rather extensively employed. Sufficient data are now at hand to permit the formulation of a perspective toward this agent as

a therapeutic measure. Park (1939) states that the apparent basis for the use of large doses of vitamin D in conditions such as chronic arthritis resides in the toxic effects of the material rather than in a physiologically beneficial replacement of a deficiency in vitamin D. The justification for this measure thus remains upon an empiric basis. Symptoms of toxicity have appeared among several of the patients subjected to this therapeutic measure. In most instances these symptoms have been mild. The toxic manifestations range from nausea, frequency of urination and nocturia to violent gastrointestinal symptoms with intense headache and profuse sweating. Comparable doses in subjects of other disorders have been seen to induce progressive hypercalcemia. Park advises great caution in exceeding the dosage of 200,000 units per day in the treatment of arthritics While it might be assumed with reason that the toxic effects are secondary to changes in calcium and phosphorus metabolism, this assumption is incorrect Observations by Reed are cited showing that while toxicity and hypercalcemia may often occur together, this parallelism does not always appear Severe symptoms may develop in experimental animals without any hypercalcemia On the contrary, both the experimental animal and man may be maintained with a high blood calcium level without evidence of comparable toxic manifestations These considerations suggest that the clinical signs of illness in the patient rather than the blood calcium level should determine whether administration of the material should be continued

As a practical rule, however, the presence of a level of calcium in the blood exceeding 12 mg. per 100 ml. should be taken as a potential danger signal. In Park's opinion, it is evident that the

influence of massive doses of vitamin D in arthritis does not depend upon its influence on calcium and phosphorus metabolism per se but rather upon an influence of a totally unknown nature, possibly lying within the region of toxic activity. In administering the drug, therefore, the effort should be made not to avoid toxic levels but rather to be certain that the injurious effect on the patient is avoided. It is apparent that the use of this agent is still upon an empirical and experimental basis.

The requirement for vitamin C in rheumatoid arthritis has been studied by Hall, Darling and Taylor in a series of 56 patients with atrophic arthritis and 12 normal subjects, observed with respect to amounts of vitamin C in the blood serum and in the urine before, during and after administration of cevitamic acid. Seventy-five per cent of the patients had subnormal levels of vitamin C in the blood. Fifty-nine per cent of the patients had a concentration of less than 0.5 mg. per 100 ml. The renal output of 4 patients maintained on a diet low in vitamin averaged less than 20 mg. per day. Six of the subjects ingesting the house diet excreted less than 50 mg. per day. The administration of 100 mg. of ascorbic acid daily for a period of 2 weeks failed to raise the level of vitamin C in the blood and was not reflected in an elevation of the urmary ascorbic acid. An increased dosage of 200 mg of vitamin C per day resulted in an increase both in the blood and urine increases in the administered quantity to 300 mg. daily failed to augment the blood level but did augment the urmary output. It is concluded that the requirement for the atrophic arthritic is between 100 and 200 mg per day

While subnormal levels of vitamin C are undoubtedly present among patients with atrophic arthritis, Hall, Darling and

Taylor failed to observe a parallelism between the vitamin C levels and the degree of clinical activity. There was no apparent improvement among rheumatoid patients placed upon a daily intake of 200 mg. per day for a period of 8 months. The significance of the increased metabolic requirement for vitamin C in arthritis as compared with normals remains undetermined.

A further study on vitamin C metabolism is reported by Rinehart. A series of 32 cases with atrophic spondylitis were found to have ascorbic acid levels of 0.12 mg. per 100 ml. blood. Ninety per cent of the cases presented levels below 0.4 mg. per 100 ml. blood. Not only were the fasting levels lower than normal but the patients showed only slight increments following the administration of 15 mg. ascorbic acid per kg. body weight. The flatness of the curve presumably constitutes evidence of undersaturation of the tissues with vitamin C. Rinehart regards this response as further evidence of a defect in the arthritic for the metabolism of vitamin C.

Additional support for the view that the arthritic state is related to vitamin C deficiency is indicated by the fact that the capillary strength was found to be low in 27 cases. Furthermore, adequate administration of ascorbic acid to 14 patients was followed by an increase in capillary resistance in 11. Twelve of 17 subjects showed decreased sedimentation rates following adequate dosage with vitamin C for a period of 4 months. Pain was diminished in all instances Rinehart concludes that there is a defect in the metabolism of vitamin C in the atrophic spondylitic and that this deficiency appears even in the presence of an otherwise normal dietary supply. While the full rôle of this defect is not yet apparent, it is held to constitute a part of the syndrome

Disturbances in protein metabolism among various classes of arthritics are shown in a study of serum proteins in rheumatoid disease by Scull, Bach and Pemberton. There are many symptoms and pathological features presented by classes of arthritics which involve deviations from the normal course of protein metabolism. Some of these are localized in the articular tissues, others are systemic. Among the former, the deposition of sodium urate, a metabolite of nucleoprotein in gout, the proliferation of the synovial membrane involving new formation of protein in atrophic arthritis, and the decrease in the physicochemical integrity of the articular cartilage in hypertrophic arthritis may be mentioned. Extra-articular disturbances in protein metabolism are evident in the secondary anemia, the peripheral edema and in the increased levels of antibodies in the serum. One or more of these features is frequently present among certain classes of arthritics. For the purpose of evaluating the extent of deviations from normal protein metabolism as reflected by modification in the serum proteins, a statistical survey was conducted

A series of 177 patients with rheumatoid disease were studied with respect to the levels of protein fractions in the blood serum. The series consists of 48 patients with severe atrophic arthritis, including 14 patients with atrophic spondylitis; 27 patients with moderate atrophic arthritis; 52 patients with hypertrophic arthritis; 34 patients with mixed atrophic and hypertrophic arthritis; 5 syphilitic, 2 tuberculous, 4 gouty subjects; 5 miscellaneous rheumatoid and 10 nonrheumatoid, and 15 normal control subjects.

Slight changes occur with respect to the total protein levels in patients with rheumatoid disease A significant number of severe atrophics, hypertrophics,

and mixed cases shows a slight reduction in the albumin levels. Severe atrophics present increased levels of globulin and decreased albumin-globulin ratios (quotients). Atrophic spondylitis is characterized by a higher level of total protein and a lower albumin-globulin ratio. The very seriously ill nonrheumatoid group presents the lowest average albuminglobulin quotient, namely, 1.05. atrophic spondylitics present an average ratio of 1.13 and the group of severe atrophics 1.27. The moderate atrophics show an average level of 1.83 which is close to that in the normals, namely, 1.99. The hypertrophic arthritics show an average value of 170 which is intermediate between the normal and the severe atrophic group and lower than the moderate atrophic group. The group of mixed cases is intermediate between the hypertrophic and the severe atrophics, a fact which is in harmony with the general clinical picture, which is likewise intermediate between the 2. The cases of gout and the miscellaneous rheumatoid diseases approximate the moderate group with respect to albumin-globulin ratio The syphilitic and tuberculous groups more nearly approximate the cases of mixed rheumatoid disease.

Interpretation of these data requires some consideration of the factors which are known to play a rôle in the production of serum proteins. It is known that infection or the presence of antigenic substances of various kinds, may lead to an increase in the level of globulin fractions The complicating influence of this factor in the present series must be considered in view of the fact that a large percentage of all the cases observed were at the time of examination, or had recently been, harboring demonstrable infective foci It is also known that under conditions of chronic plasmaphoresis, infectious factors, and breakdown of tissue

such as is involved in sterile abscesses, there may be interference with the production of albumin. This is also true of such apparently insignificant factors as the presence of viable yeast cells within the gastrointestinal tract. Such agencies may in part account for some of the lower levels of albumin encountered. There is a possibility that albumin production may also be limited not infrequently by inadequate dietary supplies of the necessary amino-acids. This rôle cannot be precisely evaluated in the present series on the basis of available data

Therapy of Arthritis of Undetermined Origin-The treatment of arthritis of undetermined origin must be individualized. However, for the sake of economy of effort practice is often codified Individual features are singled out and their relationship to therapy considered. The problem of the management of focal infection is one attracting current interest. Two points of view are expressed in current literature. On the one hand. Cecil and Angevine conclude, from an analysis of 200 cases of rheumatoid arthritis observed with respect to focal infection that chronic focal infections play a minor rôle in typical rheumatoid arthritis and that the whole question of focal infection requires reevaluation In a survey of 200 rheumatic patients conducted in 1927 Cecil found infected tonsils in 61 per cent and infected teeth in 33 per cent. Furthermore 50 per cent of the patients subjected to tonsillectomy were improved of 21 patients were improved by dental extractions The data of the recent survev provide marked contrasts with the earlier data Only 20 per cent show definite evidence of focal infection, 10 per cent show questionable foci, while 70 per cent show no evidence of focal infection This marked difference may be partially

attributed to the general betterment in oral hygiene and to the fact that many of the subjects seen in the second survey had most of the infected foci cared for prior to examination. In addition to this the criteria for the diagnosis of arthritis has been modified. The clinical material in the second series was more rigidly selected than in the first series. The group studied presented fusiform swelling of the fingers in all instances, accelerated sedimentation rates in 93 per cent and strong agglutination reactions with a strain of hemolytic streptococci in 65 per cent.

Analysis of medical histories revealed that 46 per cent of the patients had undergone tonsillectomy without apparent permanent favorable influence on the course of the disease Among 26 per cent of the patients who had extraction of teeth, 25 per cent exhibited no improvement. Those patients still requiring attention to focal infection were treated without conspicuous therapeutic The specialized approach to minor degrees of infection by the rhinologist, the urologist and the dentist is regarded as proper but subject to careful and sometimes critical interpretation. The conservative internist is inclined to treat the patient rather than the focus. The radical internist advises removal of tissues merely upon suspicion. In the light of extended experience a conservative approach is urged

The view is expressed by Traut that the general regimen for the arthritic should be more or less like that for the patient with tuberculosis. The whole mode of living requires intelligent direction and control. Regarding the treatment of focal infection, no empirical rule is applicable. The treatment of 1 tissue as a focus of infection to benefit others is justified only by experience and judgment of the physician. The finding of

enlarged lymph glands draining the area of a suspected organ is substantial evidence of involvement. The selection of time for the removal of infection requires the exercise of trained judgment. The general condition of the patient is first built up. Apical abscesses and pulpless teeth should be extracted. Pyorrheal pockets should be treated. Sinus and tonsillar infection should be given careful attention. Abnormalities in the genitourinary tract should be corrected. Particular emphasis should be placed on the correction of digestive abnormalities not only to remove possible sources of infection or toxemia but also to improve the general nutrition.

Major efforts should be made to raise the general resistance of the patient. This involves the provision of an optimally constituted diet, low in carbohydrate, liberal in proteins and vitamins Dietary supplements, including cod-liver oil, brewer's yeast, calcium and iron compounds, are often indicated. Suitable adjustments in the diet should be made to suit the dietary idiosyncrasies of the patient Heliotherapy and ultraviolet radiation are useful adjuncts to the general regimen. Parenteral therapy is regarded as making extra demands upon the resources of the system and is to be discouraged particularly in the treatment of ill nourished or organically handicapped patients.

Rest in bed for 24 hours daily is necessary during acute phases of the disease All patients require certain amount of systemic rest, depending upon the extent and the degree of activity. Local rest is further indicated for the affected joints whether the lesions are primarily due to trauma or to other causes. Joints damaged by disease should be protected from traumatic influences.

Analgesics are sometimes demanded by the condition of the arthritic. For this, acetyl salicylic acid is perhaps the drug of first choice, 5 grains (0.3 Gm.) every 2 to 4 hours. If severe diaphoresis is produced, addition of extract of hyposcyamus, ½ grain (0.02 Gm.) per dose may be used. If pain interferes with sleep, phenobarbital may be given in a dose of ¾ grain (0.05 Gm.) as a sedative.

Physical therapy constitutes an important part of the regimen for the arthritic. Heat with its attendant hyperemia is valuable for its analgesic, reparative and resorptive effects. Heat relieves pain, stiffness and induces relaxation. Heat followed by appropriate massage and exercise favors reparative processes. Light massage is first applied above and below the affected joints. These measures must be properly directed but can often be made available to the patient in the home. Postural exercises are of great value in the rehabilitation of the patient Occupational therapy is particularly useful not only for its value in providing proper exercise but also for its effect on the morale of the patient and the opportunity sometimes afforded for earning a living

The changing viewpoint toward the nature of arthritis requires as a consequence increasing emphasis upon a broad program of therapy according to Pemberton (1939). Successful treatment of patients with arthritis requires the coordinated application of a wide variety of measures The necessity for this arises from the fact that the chronic arthritic is ill, not only because of deviations within his joints but because of dislocation of physiology elsewhere within his body, viz, vascular, gastrointestinal, nervous and respiratory systems Focal infection is no longer considered as the only factor which may precipitate arthritis and is, therefore, no longer regarded as the only feature to which therapeutic

attention need be given. Recognition of this limitation does not, however, require a completely iconoclastic view toward focal infection. There is no justification for ignoring the presence of focal infection in an arthritic merely because this factor alone does not fully account for the development of arthritis.

The arthritic suffers from many functional disturbances which are open to correction. This is often recognized in respect to the milder forms of disability but is overlooked in patients who present more serious pathological symptoms. Many instances of severe classical atrophic arthritis are seen to undergo dramatic escapes from symptoms under a variety of conditions which exert influences upon physiology. The profound physiological changes associated with pregnancy, icterus, and pneumonia apparently induce a rapid reversal of the pathologic processes in atrophic arthritis. The precise mechanism by which these different states alter the pathologic processes in the arthritic are not yet clear However, they illustrate the important principle that arthritic disability is based upon functional changes which are not wholly irreversible.

Systemic rest is the most useful basic factor in the treatment and care of arthritics Appropriately managed rest affords not only 1 but several factors favoring the recovery of the arthritic. The nervous system is relieved of excessive activity. The components of this system relieved of fatigue are enabled to function more efficiently. The vascular system, which because of limitations may be inadequate to meet the requirements of activity, is enabled to supply the needs of comparatively inactive tissues. By the same token, the gastrointestinal system, often deranged, showing a decreased functional capacity, is able to supply the

nutritive requirement of the tissues of the body when at rest. These measures, valuable as they are, do not constitute a generic panacea for arthritics, but they provide many of the mechanisms necessary to a reversal of some of the deranged physiologic processes underlying many of the symptoms of the arthritic.

The clinical pattern of arthritis is not fully explained by any single factor. In this respect the problem is illuminated by deficiency syndromes wherein expenditure of energy, imbalance of foodstuffs, infection, or minor changes in gastrointestinal function may be as effective in the production of a deficiency syndrome as is a true primary inadequacy. Nutritional imbalance in the arthritic is indicated by the atrophy of bone, osteoporosis, faulty hematopoieses, altered plasma proteins and tissue edema. It is evident that these features may not arise wholly from a primary inadequacy of diet alone, but may be conditioned by some of the aforementioned factors including the presence of infectious influences and disturbances in the gastrointestinal function. An adequate therapeutic approach requires attention in several directions.

Similarly the postural and mechanical defects such as lordosis, narrowed costal angle and visceroptosis are not the causes of arthritis and their correction does not constitute a "cure." Nonetheless, such correction is essential to proper care of the patient The basis for successful therapy is a systematic attempt at readjustment of all the dislocated physiologic processes accompanying the disease. This requires precision in the direction of measures which can reach these underlying features. It demands a knowledge of how to use the components of rest: to stimulate here and sedate there: to correct deficiencies or surfeits. to discover infection or other morbid nidi

and judiciously to remove or correct them; to re-educate the patient toward his problem; to adjust somatic and local mechanics. Such physiologic equilibration constitutes an approach to specific therapy for the complex pattern of arthritis. There should be maintained at all times a balanced perspective toward all deviations presented by the arthritic and a co-ordination of physiologic influences which are capable of correcting them.

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CARDIOVASCULAR SYSTEM

By Albert W. Bromer, A.B., M.D.

Introduction—During the past few years attention has been directed to the importance of an understanding of the precipitating causes of myocardial failure in the treatment of cardiac diseases, even

before the onset of failure, the importance of rest in the treatment of congestive heart failure has been emphasized, the technic and nomenclature in connection with the precordial leads of the electrocardiogram have been standardized; the significance of paroxysmal bundle branch block has been established; the relief of anginal pain through improvement of the movement of the diaphragm—by use of an elastic abdominal belt—has been demonstrated; and the need of consideration of various factors for the proper evaluation of methods of treatment of peripheral vascular disease has been stressed.

The importance of added stress in the precipitation of congestive heart failure has long been recognized. In a study of 100 consecutive cases of congestive heart failure by W. A. Sodeman and G. E. Burch a definite precipitating cause was demonstrable in 55 (52.9 per cent) of 104 attacks. The underlying causes of failure were: Hypertension and arteriosclerosis, separately or in combination, in over 75 per cent of the group; syphilis in 10 per cent; rheumatic fever in 7 per cent; and congenital anomalies in 1 per cent. The commonest precipitating causes of congestive failure were exercise, and infection (chiefly of the upper respiratory tract); less common were pregnancy, surgical shock, psychic trauma, overeating, and alcoholism.

A study by D. Davis and H L. Blumgart of the cardiac weights of an unselected consecutive series of cases with post-mortem examination showed that coronary arteriosclerosis in itself may give rise to a slight or moderate degree of cardiac hypertrophy. Presumably impaired nutrition of the muscle fibers may cause them "to undergo stretching and consequent hypertrophy." This concept favors the "injury theory" of the causation of cardiac hypertrophy rather than the widely held "work hypertrophy theory" In patients who had suffered from congestive heart failure the weights of the hearts were considerably increased. Also, J. T. Wearn has found that the hypertrophied heart is less efficient because its capillary blood supply is relatively reduced. If the coronary vessels are already so diseased that it is not possible to accommodate the normal requirements of the myocardium, they obviously will not be able to satisfy the requirements under the conditions of exercise, and further damage to the structure is inevitable. On the basis of these observations, D. Davis has emphasized the importance of prolonged rest in the treatment of congestive heart failure.

In a program of rest treatment, thought must be given to (1) the duration of the initial period of absolute rest in bed, (2) the degree and character of reduced activity that must follow, and (3) the advisability of periodic prophylactic rest in bed. The patient with failure of severe degree, with signs and symptoms disappearing slowly, should rest in bed for a longer period than one less severely ill. After manifestations of failure have disappeared, there are 2 stages of improvement: (a) The period in which the cardiac reserve continues to increase to a certain optimum, and (b)a succeeding period—probably in the nature of organic repair—in which the gain in reserve, as measured by capacity to perform a given task, no longer shows very much change but in which the potential capacity of the heart is being increased. The longer the initial period of bed rest, the greater reduction in activity to be followed thereafter. individuals with sedentary occupation the desired effect may be accomplished by increasing the sleep and bed-rest hours, limiting stair climbing and walking, and spending the greater part of week ends in bed Prophylactic bed rest is of importance, in that the ultimate benefits to be obtained from rest are

greater when it acts to prevent failure rather than after failure has appeared.

To secure uniformity in the technic and nomenclature in connection with the precordial leads of the electrocardiogram the American Heart Association and the Cardiac Society of Great Britain and Ireland have recommended that when employing a single precordial lead the precordial electrode should be placed upon the extreme outer border of the apex beat, as determined by palpation, and if the apex beat cannot be located satisfactorily by palpation the electrode may be placed in the fifth intercostal space just outside the left border of cardiac dullness, or just outside the left midclavicular line if percussion of the heart is unsatisfactory. A single precordial lead in which the precordial electrode has this location is known as Lead IV B when this electrode is paired with an electrode in the interscapular region; Lead IV R when it is paired with an electrode on the right arm; Lead IV L when it is paired with an electrode on the left arm, Lead IV F when it is paired with an electrode on the left leg: and Lead IV T when it is paired with a central terminal connected through equal resistances of 5000 or more ohms to electrodes on each of the 3 extremities mentioned It is suggested that for all ordinary purposes Lead IV R or Lead IV F be employed In taking the precordial leads specified the galvanometer connections should be made in such a way that relative positivity of the apical electrode is represented in the finished curve by an upward deflection (a deflection above the isopotential level) and relative negativity of the apical electrode by a downward deflection.*

In certain cases of infarction of the anterior wall of the heart, multiple precordial leads are required to establish

the diagnosis. Such leads sometimes disclose abnormalities of the T deflection which would otherwise escape detection. In the differentiation of right from left bundle branch block, and in the differentiation of right from left ventricular enlargement, multiple precordial leads are indispensable. When leads from 2 or more precordial points are employed, it is suggested that the precordial electrode be paired either with an electrode on the left leg or with a central terminal connected through equal resistances of 5000 or more ohms to an electrode on the right arm, left arm, and left leg. In the first case the letters C F followed by a subscript, and in the second case the letter V followed by a subscript should be employed to designate such leads.

The position of the precordial electrode is indicated by the subscript used according to the following plan: Subscript 1 is used for the right margin of the sternum; 2, for the left margin of the sternum; 3, for a line midway between the left margin of the sternum and the left midclavicular line; 4, for the left midclavicular line, 5, for the left anterior axillary line; and 6, for the left midaxillary line. In the case of the sternal leads the precordial electrode should be placed in the fourth intercostal space, and for the other leads upon a line drawn from the left sternal margin in the fourth intercostal space to the outer border of the apex beat (or to a point at the junc-

^{*} To make the galvanometer connections in such a way that positivity of the precordial electrode will produce an upward deflection in the finished record, it is necessary to connect the left-hand wire to this electrode if the lead switch is on Lead I and to connect the left-leg wire to this electrode if the lead switch is on Lead II or Lead III To take Lead IVF, connect the left-leg wire to the precordial electrode and the left-lead switch on Lead III To take Lead IVR, connect the left-leg wire to the precordial electrode and the right-arm wire to the right-arm electrode and place the lead switch on Lead III.

tion of the midclavicular line and the fifth intercostal space) and continue around the left side of the chest at the level of the apex beat or of the junction mentioned. In the majority of cases there is no essential difference between the curves obtained when the precordial electrode is paired with an electrode on the left leg and those obtained when it is paired with a central terminal. The essential difference becomes increasingly common as the distance of the precordial electrode from the ventricular surface is increased.

That paroxysmal bundle branch block (without a short P-R interval) is as a rule a sign of serious heart disease, most often due to coronary arteriosclerosis, but in some cases associated with rheumatic heart disease, diphtheria, and factors that cannot be ascertained clinically, has been concluded by W. J Comeau, J. G. M. Hamilton and P. D. White in an analysis of 71 cases (58 found reported in the literature and 13 new cases). When conduction through the affected branch is close to a critical level, small changes in conductivity, such as may result from the increase or decrease in diastolic rest due to slight alterations in heart rate, result in sudden and complete changes in the form of the ventricular complexes

Wide QRS complexes with short P-R intervals, which are of no serious significance — which usually occur in young persons, without other evidence of heart disease, prone to attacks of paroxysmal auricular tachycardia, flutter or fibrillation — must be differentiated from the type just described. In this benigh type the reversion to the normal form may take place spontaneously, during the paroxysmal tachycardia, after exercise, or after the administration of atropine or quinidine. The rare instances of bundle branch block becoming manifest after

a prolonged period of paroxysmal tachycardia may be interpreted as indicating fatigue of one of the bundle branches due to the prolonged rapid rate; but the conduction defect is most likely to occur in individuals in whom there is heart disease.

Relief of anginal pain - presumably by more adequate filling of the heart and coronary vessels through improvement of the movements of the diaphragmaccomplished by means of an elastic abdominal support, supplemented by dietary restriction, has been observed by W. J. Kerr over a period of 4 years in approximately 100 patients. The patients were chiefly of the apoplectic type -with florid complexion and moderate or marked corpulency; all complained of orthostatic dyspnea (dyspnea only in the upright position). Fluoroscopic examination in the upright position showed the diaphragin to be 1 or 2 interspaces below the normal position; in ordinary breathing in the upright position the movements were limited, but when supine the diaphragm had a much greater excursion It was assumed that the abdominal viscera together with the increased accumulation of fat served as a counterweight suspended from the diaphragm, and that when the individual was in the upright position this weight interfered with the normal rise of the diaphragm during expiration, but in the supine position it caused the diaphragm to rise higher in the chest during expiration and acted as an aid to respiration In breathing the movements of the diaphragm aid the return of blood to the heart through alternating changes in the interpleural and intraabdominal pressures A lighter type of elastic belt has been found to afford complete relief to persons of slender build with the same syndrome

Coronary Artery Disease

Activities Associated with the Onset of Coronary Artery Occlusion -The question as to whether or not excessive physical exertion or emotion is intimately connected with acute coronary artery occlusion has received considerable attention during the past few years. In a statistical study of 817 attacks of coronary thrombosis occurring in 555 patients made by A. M. Master, S. Dack and H. L. Jaffe¹ it was found that coronary thrombosis occurred in all walks of life and in all types of occupation, and that exertion, even severe, was of little or no significance in the precipitation of an attack. Excitement, ingestion of food, infection, tobacco, alcohol, heart failure, time of day and season of vear apparently were of no significance Although 40 per cent of the attacks occurred during rest or sleep, this was probably a coincidence, since half the day ordinarily is spent in these states

Attention is called by the same authors2 to the importance of distinguishing clearly between an attack of angina pectoris and one of coronary artery occlusion. Although coronary sclerosis is the underlying pathologic condition in both angina pectoris and coronary occlusion, the former is a functional syndrome resulting from transient coronary insufficiency, whereas in coronary occlusion the myocardium is severely injured. Angina pectoris is defiintely related to exertion, meals, excitement and cold. In an attack of angina pectoris the patient usually is incapacitated for only a few minutes and is as well after the attack as before coronary artery occlusion occurs, however, the patient suffers severe, prolonged pain, may collapse, and develops signs of diminished cardiac output and heart failure: and if the attack is survived, physical incapacity persists for weeks or months.

The circumstances at the onset of the symptoms of coronary artery occlusion were discovered in 930 cases (Table I). In addition, in 200 cases detailed histories were obtained concerning the patient's activities the whole day before and even several weeks before their attacks. In 890 cases the circumstances preceding the onset of symptoms were Sleep, 22.3 per cent; rest, 31 1 per cent; ordinary mild activity, 20.2 per cent; moderate activity, 8.5 per cent; walking, 15.8 per cent; and unusual or severe exertion, 20 per cent. A correlation of the percentages with the number of hours spent daily by the ordinary person in the same occupations indicated that the circumstances were coincidental and that none of them was causally related to the coronary occlusion: that is, a coronary occlusion occurs irrespective of the state of physical activity of the body. Associated factors in 930 cases were: Meals. 9.9 per cent, emotional excitement, 56 per cent; surgical operations, 66 per cent, infection, 4.3 per cent, and miscellaneous factors, 1 per cent. It was concluded that, with the possible exception of surgical procedures, these factors did not play a rôle in the pathogenesis of coronary occlusion. Only 2 attacks of coronary occlusion were associated with trauma The belief that physical activity and excitement are not factors in the onset of coronary occlusion was confirmed also by detailed histories of the activities and emotional states of patients for hours, days and weeks preceding attacks. Sixty patients sustained an attack of coronary occlusion after having been bedridden for weeks or months because of some chronic illness. attacks were well distributed throughout all the hours of the day, with peaks at 2 A M and 10 P M, which fact also

TABLE 1
Types of Activity at Onset of Coronary Artery Occlusion (930 Attacks)

	Types of Activity	Number	Percentage
. Prima	ry Activities (890 attacks):		
1.	Sleep	198	22.3
2.	Rest—lying down or sitting up	277	31.1
3.	Ordinary mild activity. 62, in home (dressing, standing, walking about, playing with children, talking, retiring, etc.); 35, in store or office; 14, sitting in car or train; 9, in doctor's office or clinic; 8, doing light housework; 6, getting out of bed; 5, taking showers or bath; 5, getting out of bus or car; 5, playing cards; 4, attending a meeting; 4, sitting in a movie; 2, in restaurant; 21, miscellaneous.	180	20.2
4.	Moderate activity (except walking) 35, working as laborers (painter, engineer, carpenter, baker, tailor, presser, etc.), 16, driving car; 8, during bowel movement or straining at stool, 6, shopping, 2, coughing, 2, running upstairs, 2, during coitus	76	8.5
5	Walking 107, in street, 11, upstairs, 6, after meals; 5, against cold wind, 4, uphill, 4, downstairs, 2, in snow-storm, 2, carrying ten pounds.	141	15 8
6	9, during or immediately after sport or games (football, swimming, dancing, skating), 5, lifting or moving a heavy load; 3, running for train; 1, after long automobile ride	18	20
	nated Factors (930 attacks): . Meals . Meavy meal, 33, ordinary meal, 22, light meal, . 15, in sleep, 10, while walking	92	g g
2	Excitement 13, gambling or playing cards, 8, during argument, 4, at movies, 3, news of deaths of relatives, 3, fright, 3, at wedding or banquet, 2, making speech, 2, during coitus, 1, at funeral, 13, miscellaneous (emotional upset)	52	5 6
3	Surgical procedures 26, laparotomy, 20, genitourinary operation, 7, eye, ear, nose or throat operation, 3, kg operation, 2, thyroidectomy, 1, thoracotomy, 1, tooth extraction, 1, incision of furuncle, 1, para- yertebral block, 1, bronchoscopy	63	66
4	Infection 14, upper respiratory infections, 6, grippe, 4, cholecystitis, 2, peritonitis, 3, pyclonephritis, 4, pneumonia, 2, appendicitis, 2, sepsis, 3, abdominal suppuration	40	4-3
5	Miscellaneous 3, diabetic acidosis, 2, insulin injections, 2, trauma (1 fall on chest and 1 injury to eye), 2, smoking, 1, typhoid injection	10	1 1

indicates that activity is not a factor in the precipitation of coronary occlusion. Premonitory symptoms, such as chest pain, dyspnea or weakness, were present in 80 of 170 cases in which these symptoms were investigated.

In the minds of the authors there is no evidence that physical effort or ex-

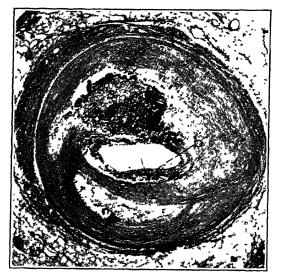


Fig 1—Case 5584—A section through the descending branch of the left coronary artery, showing massive hemorrhage, a, into the vessel wall. The endothelial lining, b, is intact, and the lumen, c, is patent (Wartman Am Heart J)

entement produces intimal hemorrhage in the coronary arteries—which is the usual forerunner of thrombosis and occlusion Intimal hemorrhage is the end result of the progressive, degenerate arteriosclerotic process and is probably a fortuitous event—It was found at necropsy as frequently in patients who had been bedridden prior to the occlusion as in those who were physically active

Relation of Physical Exertion and Emotion to Precipitation of Coronary Thrombi—In 31 of 36 consecutive fatal cases of coronary thrombosis, in which the structure of the occluding thrombus was studied in serial sections, hemorrhagic foci were found in the in-

tima at the site of thrombotic occlusion by J. C. Paterson.³ It is his belief that 2 principal factors are involved in the mechanism of capillary rupture: (1) Softening, by atheroma, of the tissues surrounding and supporting the capillary wall, and (2) high intracapillary blood pressure Thus, high coronary blood pressure, the result of strenuous exercise or emotion (or of persistent hypertension), is 1 of the underlying causes of capillary rupture and intimal hemorrhage in arteriosclerotic coronary arteries. And if conditions are favorable, the various changes which result from capillary rupture may then be the initiating factors in the deposition of coronary thrombi

The subject of intramural coronary arterial hemorrhage has also been studied by M. C. Winternitz, R. M. Thomas and P. M. LeCompte⁴ and by W. B. Wartman.⁵ The latter investigator has described 6 cases of complete occlusion of sclerotic arteries by intramural arterial hemorrhage without thrombosis, the actual occlusion of the vessel resulting from a hematoma formed entirely within the wall of the vessel (Figs. 1 and 2)

W B Cooksey 6 feels that atheromatosis is the basic cause of coronary artery occlusions. And is it not logical to assume that considerable strain may bring about the breaking of a portion of the hard atheromatous area or the rupture of a tiny subintimal vessel which may give rise to tissue substance which might constitute the nucleus of platelet agglutination leading to the formation of thrombosis? A small subintimal hemorrhage or tear in the hardened wall may not be demonstrable by the time a postmortem examination is done. Furthermore, it is well established that an individual's physiologic response to exercise depends a good deal on his physical training. The well-trained athlete shows

relatively little change in pulse rate and blood pressure as compared to a sedentary individual in poor physical training. Also with severe sudden physical exertion there is sometimes an extreme elevation in blood pressure, but more often a considerable drop occurs after an initial rise. The fall of pressure can produce a disturbance in the coronary flow, and in sedentary individuals who overexert themselves there can be produced-with a combination of fall in blood pressure and an unduly accelerated heart—a very possible coronary stasis; and, in line with this possibility, the small nucleus of platelet agglutination in the presence of stasis can bring about thrombosis.

Angina Pectoris and Cardiac Infarction from Trauma or Unusual Effort — Evidence from the literature and from his personal experience that angina pectoris and cardiac infarction may be brought about by unusual effort or by trauma is presented by E. P. Boas.7 Attention is called to the recent monograph of E. Warburg⁸ in which are presented 174 instances of myocardial lesions due to nonpenetrating traumatic injuries to the chest abstracted from the literature and 13 of Warburg's own cases, and to the reports of other authors who believe that symptoms of angina pectoris may be initiated by traumatic nonpenetrating injuries to the precordial region of the chest. In the experience of G Fitzhugh and B E. Hamilton9 "more often than not fatal anginas or coronary occlusions were immediately preceded by unusual departures from ordinary habits of living." And in a recent study of 1640 attacks of coronary occlusion W. B. Bean and C A Mills¹⁰ found that in northern cities such attacks occur with greater frequency in winter than in summer; there were twice as many attacks in Jan-

uary as in August; and they concluded that the greater frequency of infection and the heightened metabolism in cold weather increase the work of the heart and so add to the hazards to which these patients are exposed. Boas has examined and studied 25 patients in whom coronary occlusion appeared to have been



Fig 2—Case 5584—A section 3 mm distal to Fig. 1 The lumen, c, is occluded because of compression by the intramural hemorrhage, a The endothelial lining, b, is intact, and there is no thrombus (Wartman: Am Heart J)

directly induced by severe or unusual exertion.

The anatomic studies made by Paterson, Winternitz and Wartman suggest how unusual exertion may bring about coronary artery occlusion. "With physical effort there is a sudden alteration of arterial pressure, cardiac action is increased, rupture of one of the capillaries or sinusoids in the arterial wall may occur, or a softened atheromatous plaque may rupture into the arterial lumen. If the hemorrhage is large there may be almost immediate occlusion of a coronary artery, if the hemorrhage is small or slow, or if it is followed by a gradually growing mural thrombus the occlu-

sion may develop slowly or remain incomplete. Thus the concept of coronary occlusion and of angina pectoris induced by physical exertion established by discriminating clinical observation finds support and confirmation in dissections of diseased arteries. It follows that when symptoms of coronary artery disease are induced by physical strain, even when the patient has had no preceding symptoms, there have most likely been antecedent anatomic lesions of the coronary arteries. When such symptoms follow nonpenetrating blows to the precordium no such preexisting arterial disease need be predicated" The question as to whether the particular injury or effort was a competent producing cause of the symptoms can be answered only by careful evaluation of the succession of events in each individual case, with due recognition of the fact that patients tend to ascribe their illnesses to some unusual experience which actually may have no significance.

Boas states "To relate an accident or an unusual effort to a subsequent coronary thrombosis or syndrome of angina pectoris one must predicate cardiac symptoms accompanying or immediately following the event to which the cardiac mjury is ascribed. If the symptoms are immediately disabling the causal connection is clear. If a lapse of days occurs between the causal event and the complete disablement there must be a continuity of symptoms dating from the When an unusual strain during work is followed by cardiac disability in the sense outlined, and when this occurs in a person who has been previously well and free from symptoms while at work, it is proper to conclude that the disability was induced by the work and is therefore compensable."

Postoperative Coronary Artery Occlusion—The extent of the risk of sur-

gical operation in the presence of severe coronary artery disease has been investigated by H. J. Brumm and F. A. Willius¹¹ in a study of 257 cases (presenting coronary atherosclerosis with the anginal syndrome or with healed myocardial infarcts with or without recurrent angina) who underwent major surgical operations at the Mayo Clinic. One hundred fortyeight patients (57.6 per cent) were 60 years of age or older; the youngest patient was 35, the oldest 83, and the average age of the entire group was 603 years. There were 186 men and 71 women, a ratio of 2.6:1. Electrocardiographic abnormalities, which included significant T-wave negativity, incomplete and complete bundle branch block, complete heart block and auricular fibrillation, were present in 504 per cent of the cases. Previous coronary thrombosis with healed cardiac infarction had occurred in 32 cases (124 per cent); and wellmarked hypertension was present in 100 cases (389 per cent) Eleven patients in the series (43 per cent) died from cardiac causes In 7 instances, death resulted from coronary thrombosis; in 2, from congestive heart failure, and in 2 it occurred abruptly without apparent thrombotic occlusion (Table 2)

Of 47 patients who underwent operations on the gall-bladder and biliary passages, death due to congestive heart failure occurred in 2 instances while the patients were still in the hospital. The 2 fatal cases were examples of marked obliterative coronary atherosclerosis with the anginal syndrome in which severe recurrent biliary colic associated with cholelithiasis made surgical intervention imperative; the myocardium of each showed marked myofibrosis. Of 18 patients who underwent operation on the stomach and duodenum, 1 cardiac death occurred, a male, aged 60 years, with a

TABLE 2
(TIMICAL DALL ON THE 11 PATIENTS DYING FROM CARDIAC CAUSES

1 1	Condition Found at Postmortem Examination	Acute infarct of the left ventricle, anterior; coronary selerosis (3)	Acute infarct of the left ventricle, anterior, coronary selerosis (3)	Acute infract of the left ventricle, anterior; coronary sclerosis (3)	None	None	Acute infarct of the left ventricle, anterior; coronary sclerosis (3)	Coronary selerosis (3) with extensive myofibrosis of the left ventriele	Coronary sclerosis (4) with dilatation of the left ventricle and mural thrombosis	Acute infarct of the left ventricle, anterior; coronary sclerosis (3+)	Acute infarct of the left ventricle: coronary sclerosis (4)	Coronary sclerosis (3) with extensive healed infarct of the left ventricle.
	Day of Death (Post- opera- tive)	2	8	ю	35	35	-	=	25	В	-	C
	Mode of Cardac Death	Coronary	Coronary thrombosis	Coronary thrombosis	Coronary thrombosis	Coronary thrombosis	Coronary thrombosis	Congestive heart failure	Congestive heart failure	Suddendeath	Coronary thrombosis	Sudden death
	Electrocardiogram	Incomplete bundle branch block, Twave negatively in lead 1	Diphasic T waves in lead 1	Normal	T wave negativity in lead 1	T wave negativity lead 1, ventricular escape	Normal	Normal	Normal	Normal	Diphasic T waves all leads	T wave negativity lead 1
	Duration of Anginal Syn-thome, Vears	V	9	~ 1		^1	-		~1	+	- rc	۳. د
	Mesthesia	Nitrous oxide, ether	Regional and nitrous oxide	Spinal	Infiltration and nitrous oxide	Infiltration and nitrous oxide	Infiltration and introus oxide	Spinal	Ether	Ether	Nitrous oxide	Regional and ntrous oxide
	Operation	Repair of diaphrag- matic herna	Partial gastrectomy and duodenostomy	Cystostomy and exploration for carcinoma of urnary bladder	Thy roadectomy	Thyroidetomy	Thy roidectomy	(holeeystectomy	(holecy stectomy	Resection of sigmoid for caremoma	Posterior nerve root resection	Bilateral cervico- thoracie ganglion- ectomy with resec- tion of their trunks
-	Age Sev	^r o	' 0	Ç	O >	-	•	*5	O+	* s	* 2	*r_
!		52	9	02	5	50	2	99	 85	6.2	57	37
-	, d5(1	~	m	4	v	σ	7	×	0	2	=

(Brumm and Willus J A M A)

chronic perforating ulcer of the duodenum with partial obstruction in whom coronary thrombosis developed 3 days after operation. The risk of operation was well appreciated by the patient and all concerned, as the anginal syndrome had been suffered for 10 years. Of 42 cases undergoing thyroidectomy, death from coronary thrombosis occurred in 3 instances. No cardiac deaths followed 63 cases of transurethral prostatic resection, 10 operations on the breast, and 12 gynecologic operations. One cardiac death followed 26 urologic operations, excluding transurethral prostatic resection; 1 occurred after 8 miscellaneous abdominal operations, and 2 after 18 miscellaneous operations, such as sympathetic nerve resections, amputation of the leg, excision of a parotid tumor, etc.

The cardiac mortality in this group of cases is remarkably low. But-it is stressed by the authors-that fact should not instill false optimism into the clinician or the surgeon, because it must be realized that this accomplishment is not of casual origin but the result of careful preoperative study, expert administration of anesthetic agents, and skillful surgical technic and judgment. The time element in the surgical procedure is of extreme importance, for the shorter the time of operation and anesthesis, the less marked is the added load imposed on the cardiovascular system. Also, gentleness in the manipulation of organs and tissues lessens the danger of surgical shock, which in itself may tilt the balance away from recovery And of paramount importance is the surgeon's determination to limit the operation to the procedure planned in advance and to avoid undertaking additional operative steps that might be permissible in the patient without heart disease. That is, surgical procedures not of importance are to be condemned as unwise and extremely hazardous in the presence of advanced coronary artery disease.

Drug Therapy in Coronary Artery Disease—In discussion of the use of drugs in coronary artery disease, H. Gold¹² emphasizes that the chief objectives toward which therapy is directed are: (a) Pain; (b) nervous symptoms — apprehension, anxiety, and restlessness; (c) congestive heart failure; (d) paroxysmal dyspnea; (e) shock, and (f) disorders of heart rhythm (auricular fibrillation or flutter, ventricular tachycardia); and that the agents most frequently employed are nitrites, xanthines (theobromine and theophylline), opium alkaloids, sedatives. digitalis, diuretics, quinidine, oxygen, papaverine, iodides, tissue extracts, and emergency measures.

Nitrites—In the treatment of the pain of effort angina, nitrites are the drugs of choice, effecting benefit through dilatation of all the peripheral arterioles, including the coronary vessels Their use is not entirely free from disagreeable effects. e q, headache, sensation of throbbing and tension in the head, palpitation and, in excessive doses, collapse. The dose should be administered at the first suggestion of the attack of pain rather than to wait for its full development; and if the first dose does not bring relief within 5 minutes, it may be repeated as many times as necessary at intervals of 5 minutes until either the pain subsides, or headache appears to preclude its further use at that particular time. In cases with extremely frequent attacks of pain coming on with the slightest provocation, even while at rest, the use of a tablet or 2 of glyceryl trinitrate (nitroglycerin) regularly at intervals of about 2 hours often will considerably reduce the number of attacks or even abolish them. Frequent use of the nitrites over a period of time does not lead to dependence on them nor to reduction of their efficacy.

In the pain of the acute stage of coronary thrombosis, the nitrites only occasionally afford relief. There is some hazard in their use at that time since they infrequently through fall of blood pressure stimulate the cardiac accelerator mechanism, which may precipitate dangerous ectopic tachycardia and by further lowering the blood pressure—which may already have fallen considerably - may impair the blood flow to the rest of the myocardium. However, in cases in which the arterial pressure remains high during the early stage of thrombosis and recurring attacks of pain take place, the nitrites may prove helpful.

The most satisfactory preparation of the nitrites is the tablet triturate of glyceryl trinitrate, of which the average dose is $\frac{1}{150}$ grain (0.4 mg.) dissolved under the tongue The perle of amyl nitrite, commonly used by inhalation, on the whole is not so satisfactory as the tablet of glyceryl trinitrate in that the amount actually inhaled varies greatly. Furthermore, the drug is absorbed from the lungs more rapidly than glyceryl trinitrate from the sublingual tissues, producing more violent effects; and the dose of 5 minims (03 cc.) in a perle sometimes causes alarming symptoms in individuals who are overly careful in allowing little or none of it to escape Erythrol tetranitrate, 12 gram (0.03 (.m.), at bedtime proves helpful as a prophylactic measure when attacks of pain are likely to occur during the night.

Xanthines—The purine bases, particularly theobromine and theophylline (most widely used in the form of double salts, e.g., with sodium acetate or sodium salicylate, or in combination with ethylenediamine), are extensively employed in the treatment of coronary artery disease. But in the opinion of Gold, these preparations are of questionable value in the relief of cardiac pain. In a study

of 100 selected cases of effort angina made by Gold and his coworkers, 13 it was found that no more relief from cardiac pain was obtained from these compounds than from sugar of milk administered in similar manner. However, the xanthines are valuable as diuretics in congestive heart failure; and intravenous injections of 3¾ to 7½ grains (0.25 to 0.5 Gm.) of theophylline ethylenediamine (aminophylline) bring about dramatic relief of the respiratory depression occurring with Cheyne-Stokes respiration in the course of cardiac or renal failure

(In a study of the effect of different drugs in angina pectoris, made by J. E. F. Riseman and M. G. Brown¹⁴ in 1937. it was found that under standardized conditions with exercise consisting of repeatedly mounting and descending a 2step staircase, glyceryl trinitrate administered beforehand prevented attacks and enabled many patients to do considerably more work, one-half of the patients were benefited by aminophylline in doses of 3 grains (0.2 Gm.) and by quinidine sulfate in doses of 5 grains (0.3 Gm.), 4 times daily; and theophylline calcium salicylate, erythrol tetranitrate, and atropine sulfate often were of value—occasionally benefiting patients not helped by either ammophylline or quinidine sulfate. The exercise tolerance test revealed that patients whose treatment consisted of lactose, sodium bicarbonate, potassium iodide, or tissue extract were unable to perform any more work than was possible without medication But when the efficacy of treatment was ascertained by the usual clinical methods, with judgment based solely on the patient's estimation of therapeutic benefit, all the drugs administered were approximately equal in value-that is, placebos were just as often beneficial as

the xanthines and other medicaments.
—ED.)

Morphine—In the classic case of coronary thrombosis with agonizing pain, anguish and fear of impending death, morphine is the drug of choice. Its beneficial effects arise not only through the relief of pain but through the fact that it abolishes a disposition to move about, and in many instances gives rise to a sense of well being. At times pain may be so severe that even morphine is not entirely effectual in bringing relief. In such instances, the sharp edge of the pain should be dulled by repeated safe doses; and then, after a period of several hours, the pain subsides—partly as the result of its natural course independent of the drug. But to attempt to abolish the pain completely may give rise to dangerous depression of respiration Not all patients with coronary thrombosis require large doses of morphine; many require no morphine It is important to bear in mind that the 3 major indications for its use in the course of coronary thrombosis are severe pain, its attending anxiety, and the distress of paroxysmal dvspnea

The course of coronary thrombosis sometimes is complicated by the administration of morphine, in that it promotes constipation with abdominal distention and urinary retention through spasm of the bladder sphincter Furthermore, it may occasion vomiting which, through the violent muscular effort entailed, may prove a source of danger, and also confusion might arise as to whether the vomiting is due to the drug or to the coronary thrombosis itself. Morphine through strong vagal stimulation also renders the heart more susceptible to ventricular ectopic rhythm. Morphine poisoning is more likely to occur in cases in which large doses of the drug appear to be necessary for the relief of agonizing

pain, if the pain subsides spontaneously before any appreciable amount of the drug has been excreted; older patients are more sensitive to this phenomenon. Pain is an antidote to morphine poisoning.

In the majority of cases, $\frac{1}{4}$ grain (0.016 Gm.) of morphine sulfate may be administered subcutaneously and repeated at intervals of one-half hour until the pain is abolished or reduced to a minimum. The interval between doses should not be shorter; and to administer more than 1 grain (0065 Gm) in 12 hours is rarely wise. Codeine in doses of $\frac{1}{2}$ or 1 grain (0.03 or 0.065 Gm.) may often be used to advantage in the milder cases of coronary thrombosis. If moderate pain persists over several days. the danger of disagreeable withdrawal symptoms is greatly minimized by the substitution of codeine for morphine Dilaudid, a synthetic derivative of morphine, is about 5 times as potent, and may be used in place of morphine in dosage of $\frac{1}{20}$ grain (0003 Gm); but it is doubtful whether it has any advantages over morphine It must be used as cautiously as morphine in view of the likelihood that it also is habit forming. Pantopon, a preparation containing the total alkaloids of opium, is rather widely used. but there is no satisfactory pharmacologic or clinical evidence that it exerts any effects other than those due to the morphine it contains 15 When intolerance to morphine exists, a combination in capsule of $\frac{1}{2}$ or 1 grain (0.03 or 0.065) Gm) of code with $\frac{1}{150}$ grain (0 0004) Gm) of scopolamine hydrobromide will occasionally prove a satisfactory substitute. And when pain is resistant to other measures, placing the patient in a tent with oxygen of about 50 per cent concentration frequently is useful, being particularly applicable in the presence of cyanosis

Barbiturates—Members of the barbituric acid series, such as phenobarbital, barbital, amytal, or pentobarbital sodium, are the most popular sedatives in the management of patients with coronary artery disease. By reducing nervous excitability, they are effective in reducing the number and severity of the attacks of effort angina, and through control of fear and anxiety they diminish the distress and restlessness which involves a dangerous expenditure of physical energy in acute coronary thrombosis. Experimental studies 16 have shown that these drugs reduce the susceptibility of the heart to ectopic rhythms, thereby aiding in the prevention of ventricular tachycardia which occasionally constitutes a serious complication. As a rule, it is not well to exceed from $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.016 to 0.03) Gm.) of phenobarbital 3 times a day, or from $\frac{34}{4}$ to $1\frac{1}{2}$ grains (0.05 to 0.1 Gm.) of pentobarbital sodium or analogous doses of some of the other members of the group, since large doses not infrequently cause a form of stupor associated with motor unrest. If such a state has been produced, the drugs must be discontinued for a day or 2 until sufficient elimination has taken place to reestablish the patient's normal control.

Digitalis—There are 2 general indications for the use of digitalis in coronary artery disease. (1) Cardiac failure, and (2) certain disorders of rhythm with or without cardiac failure, 212, auricular fibrillation, auricular flutter, and possibly paroxysmal tachycardia Clinically, primary myocardial failure manifests itself in 2 general forms, which may occur singly or in combination: (a) "Congestive heart failure," which follows failure of the right ventricle, is manifested by dyspnea, orthopnea, distended veins of the neck, enlarged liver, pulmonary congestion, edema, and ascites; and (b) left ventricular failure is characterized by dyspnea on exertion and often pulmonary râles, and at times by recurring paroxysms of dyspnea or pulmonary edema (which not infrequently occur at rest).

(As a rule, the heart does not fail as a whole simultaneously—that is, 1 ventricle usually begins to fail before the other. Failure of the left ventricle occurs as a primary manifestation of myocardial insufficiency more often than does failure of the right ventricle, in that the causes of left ventricular strain, viz., arterial hypertension, aortic valve disease, and myocardial infarction, are relatively commoner than mitral stenosis, chronic pulmonary disease, and congenital pulmonary stenosis—the causes of primary failure of the right ventricle. Actually, however, the commonest cause of failure of the right ventricle is insufficiency of the left ventricle—with the resultant back pressure in the pulmonary vascular circuit.—ED.)

In the early stage of coronary thrombosis, manifestations of myocardial failure are of relatively rare occurrence; and therefore there is no indication for the use of digitalis. The distinction of right or left ventricular failure from peripheral circulatory failure often presents great difficulties; many cases show temporary equivocal signs, such as inconstant râles at the base of the lungs. In the absence of auricular fibrillation, auricular flutter and paroxysmal tachycardia, it is well to withhold digitals until unmistakable clinical indications of right or left ventricular failure appear.

Digitalis does not exert any direct constrictor action on the coronary circulation in patients with coronary artery disease—as has been shown by Gold and his coworkers¹⁷ in a study of 120 selected cases of effort angina, nor is there any danger of rupture of the heart resulting from its administration

A schedule of dosage in the average case of auricular fibrillation or heart failure in coronary thrombosis is about 4 cat units of digitalis leaf daily for 3 days, followed by about 2 or 3 cat units a day until optimum therapeutic benefit is attained; and then a daily maintenance dose of 1 or 2 cat units should be continued. Toxic manifestations should be avoided.

The patient should be watched carefully for the appearance or increase in the number of ventricular premature beats, which should serve as a guide to reduction of the dose.

Diuretics—Diuretics are useful in the control of congestive heart failure and attacks of paroxysmal dyspnea An intravenous injection of 1 cc. of salyrgan or mercupurin 2 or 3 times a week, with or without a daily dose of 75 to 90 grains (5 or 6 Gm) of ammonium nitrate, often proves very helpful in conjunction with digitalis

Quinidine—Quinidine is useful in the treatment of frequent premature contractions and of auricular fibrillation, auricular flutter, and ventricular tachycardia Ventricular tachy cardia is the arrhythmia most feared after coronary thrombosis, particularly the most severe grades in which the heart rate may rise to 250 beats per minute. To patients presenting premature ventricular contractions after coronary thrombosis, an oral dose of 5 grains (03 Gm) of quinidine sulfate may be given 3 times daily, and the dose may be increased if necessary 5 grains (03 Gm) daily until the abnormal beats disappear or until minor toxic symptoms appear It is well to bear in mind that auricular fibrillation or flutter caused by coronary thrombosis usually subsides spontaneously within hours or days, and unless the rate is extremely rapid and appears to impair the circulation, the condition may safely be allowed

to run its spontaneous course. Quinidine should be used only for the periods necessary to expedite the restoration of the normal rhythm. If signs of congestive failure are present, digitalis is preferable to slow the ventricular rate in auricular fibrillation and to restore normal rhythm in auricular flutter Intravenous administration of quinidine is dangerous, and should be used only in extreme emergency and by those familiar with its use.

Papaverine, Iodides, and Tissue Extracts — Papaverine in $\frac{1}{2}$ or 1grain (003- or 0.065-Gm.) doses exerts a mild general depressant action, and in animal experiments relaxes smooth muscle. But for the control of cardiac pain it appears to have little value. While iodides are extensively employed in the treatment of coronary sclerosis, there is no evidence that they influence the symptoms or the course of the disease process in the absence of syphilis. Tissue extracts are widely exploited as "heart hormones" for the treatment of angina pectoris: but there is lack of evidence to substantiate their value.

Emergency Measures—Emergencies arising in the course of coronary thrombosis, in which drug therapy is extremely difficult to evaluate, are Shock, acute pulmonary edema, Adams-Stokes syndrome, and acute collapse at the onset of an attack in which the pulse disappears and consciousness is lost Epinephrine is occasionally helpful in acute pulmonary edema if the systolic pressure is low, and in Adams-Stokes attacks; but the danger of precipitating ventricular tachycardia must be borne in mind. Posterior pituitary substance should not be used for its vasopressor effect, because of the constrictor action on the coronary vessels Caffeine, metrazol, coramine, intravenous dextrose solutions are widely used in the peripheral failure of coronary thrombosis; but there are no satisfactory clinical studies to prove their usefulness. It is well, however, to keep in mind the value of coramine, metrazol and caffeine in the event of respiratory depression which might result from overdosage of morphine.

In conclusion, Gold emphasizes the fact that while in many instances great suffering is spared and a life is saved through the judicious use of drugs in coronary artery disease, the major part in the treatment lies not in drugs but in expert guidance in making the mental and physical adjustments which will enable these patients to carry on within their capacity without symptoms.

Drug Treatment of Angina Pectoris Due to Coronary Artery Disease-In a study of the effect of 16 drugs, including a placebo (milk sugar) on angina pectoris due to coronary artery disease, made by A. M. Master, H. L. Jaffe and S. Dack¹⁸ on 116 ambulatory patients attending the angina pectoris clinic at the Mount Sinai Hospital, New York City, and on 85 private patients, no drug was found to exert any specific effect on the anginal syndrome. drugs included several xanthine derivatives, sedatives, such as phenobarbital. chloral, and bromides, the nitrites, alcohol, a pancreatic hormone, digitalis, and 2 narcotics, codeine and dilaudid best results were obtained with the placebo, and the number of patients improved ranged between 15 and 30 per cent for all drugs No drug was consistently successful in a significant number of cases, some patients were helped by all drugs, others by none Frequently, dispensing a new drug gave relief for a time, but this usually wore off until another drug was substituted

The beneficial effects attributed to many drugs in the past may be explained on the basis of insufficient consideration of the significance of the natural course of the anginal syndrome, and particularly of psychologic factors in determining the degree of pain. Patients not infrequently have spontaneous remissions of anginal attacks for varying periods in the absence of medication. And often a patient will volunteer the information that for no obvious reason at all he has felt much better during the preceding week or 2; and such an improved state may continue. The occurrence of anginal pain is intimately related to numerous events in the daily life of the patient, such as the amount of exertion, the diet, the presence of constipation, the weather; and a change in any of these may influence the number and severity of attacks. Of paramount importance are the nervous make-up and emotional status of the patient. Not uncommonly, a diminution in domestic or financial difficulties or some encouraging event lightens a hitherto persistent anginal syndrome. In practice, sedatives, because of their quieting influence, have proved slightly more effective than other drugs.

The conclusion is drawn by the authors that drugs should play a minor rôle in the treatment of angina pectoris. Instead attention should be directed to rest, dietary restriction and careful consideration of the mental and emotional status of the patient. The physician who spends half an hour talking to a patient, gaining his interest and confidence, is most apt to help the patient

Pharmacology of Cheyne-Stokes Respiration—In a study of the pharmacology of Cheyne-Stokes respiration by M. H. Nathanson and J. P. Fitzgibbon, 19 theophylline ethylenediamine (aminophylline) was found to be more successful than any other drug in abolishing the periods of apnea or hyperpnea. Coramine in 2 cc. doses proved without effect on the respiratory disturbance in 3 patients who responded to 3¾ grains

(0.24 Gm.) of aminophylline intravenously. And benzedrine sulfate, an adrenalinlike substance which has an intense stimulating action on the central nervous system, in dosage of ½ grain (0.01 Gm) intravenously failed to abolish the cyclic breathing in 3 patients who had been benefited by aminophylline. Caffeine sodium benzoate in dosage of 9 grains (058 Gm.) had no effect on the respiratory disturbance of 2 patients, while aminophylline showed its characteristic action; in 1 case normal breathing was brought about for 20 minutes, whereas aminophylline restored normal respiration for several hours.

That the effective substance in theophylline ethylenediamine is theophylline, that ethylenediamine itself is ineffective, and that theophylline with other combinations shows its characteristic effect in Cheyne-Stokes breathing has been demonstrated. However, the exact mode of action of theophylline on Cheyne-Stokes breathing is not clear. A direct action on the respiratory center is extremely unlikely, but it is possible that it acts on the cerebral circulation, as suggested by the reduction in intrathecal pressure observed by W. D. Paul, J. A. Greene and A. E. Feller.

Cyclic breathing, with its attendant subjective distress, may occur relatively early in the course of heart disease, and in some instances the restoration of normal breathing gives not only subjective relief, but also, by permitting the necessary rest, is an aid in relieving cardiac failure. In such cases a dose of 33/4 grains (0.24 Gm) of theophylline ethylenediamine intravenously should be given trial, and if it fails or if the duration of normal breathing is short, a dose of 71/2 grains (048 Gm), dissolved in 20 cc. of water, should be given, allowing 3 to 5 minutes for the injection set of the action is immediate, and the duration in the usual case is many hours. Unpleasant reactions, consisting of tachycardia, flushing of the face, sweating and nausea occur in only a few instances. When cyclic breathing returns, administration of the drug should be repeated; usually not more than 2 or 3 doses a day are necessary. In a small group of patients suffering from nocturnal respiratory distress, special enteric-coated tablets of a theophylline compound administered by mouth in dosage of 3 grains (0.2 Gm.) at 6, 7, and 8 P. M. prove of value in promoting restful sleep, making it possible to discontinue the use of sedatives.

Left Ventricular Failure

Definition and Pathogenesis—D. E. Bedford²¹ states that in clinical terms left heart failure implies pulmonary engorgement behind a weakened left ventricle, without systemic venous congestion and its consequences, and with a normal venous pressure. The recognition of isolated left heart failure is of practical importance because pulmonary edema requires prompt treatment by venesection, digitalis and diuretics—without waiting for the appearance of dropsy.

The syndrome of left-sided failure is best explained in terms of the back-pressure theory first explained by James Hope in 1839 The heart actually "comprises 2 separate pumping units, right and left, between which is interposed the lungs, which, by virtue of their ready capacity to take up additional blood, play an important part in the mutual adjustment of the 2 sides of the heart mally, these 2 pumps work in exact harmony, the left ventricle quickly adapting its output to correspond to the volume of blood delivered to it by the right, which thus sets the pace. But, when as happens in certain pathological states, the left ventricle is overburdened, it may

fail to keep pace with the right, with the result that blood accumulates behind it. in the lungs." Intensification of the pulmonary congestion by the recumbent posture or by effort may excite paroxysms of dyspnea, known as cardiac asthma. Recumbency increases the blood content of the lungs and diminishes the vital capacity, thus increasing pulmonary congestion-which during sleep may pass the threshold that would normally excite cough and expectoration, until eventually sleep is broken and the paroxysm of dyspnea takes place. Cough is an important factor in aggravating pulmonary congestion. (Coughing produces an increase in respiratory rate which accelerates the return of venous blood to the right side of the heart, which in turn increases the pulmonary congestion, thereby promoting the possibilities for continuation of coughing. A vicious cycle may be instituted which, unless interrupted, may progress to pulmonary edema and end fatally.-ED) Left ventricular failure of severe degree gives rise to acute pulmonary edema; and pronounced left ventricular failure often eventually leads to failure of the right ventricle with engorgement of the neck veins, peripheral edema, enlargement of the liver, and possibly ascites and anasarca.

Incidence and Etiology—All but 17 of the 154 patients in Bedford's series were consecutive cases seen in practice. There were 119 males and 35 females—a ratio of just over 3-1, corresponding closely to the sex-incidence of angina pectoris, the ages ranged from 35 to 82, the average age at the onset of symptoms being 60½ years. Three common forms of heart disease predispose to left ventricular failure—namely, hypertension, coronary arteriosclerosis, and aortic disease, of which hypertension is predominant. Of the 132 patients with paroxysmal dyspnea, 111 (84 per cent)

had arterial hypertension; angina pectoris or coronary thrombosis was present in 54 cases (41 per cent), of which 43 also had hypertension; aortic disease was present in 21 cases (16 per cent), 18 of whom had aortic insufficiency and 3 aortic stenosis. In the nonparoxysmal group of 22 cases, coronary thrombosis occurred in 18, arterial hypertension in 12, and aortic insufficiency in 1.

Left ventricular failure and angina pectoris are found in the same etiological types of heart disease—often in the same patient, when the dyspneic usually succeeds the painful phase. In coronary thrombosis pain and dyspnea may occur simultaneously, and acute pulmonary edema at times develops within a few hours of the onset of pain. Apart from coronary thrombosis, pulmonary edema may follow any severe attack of angina pectoris, especially the nocturnal type and in syphilitic cases. As observed by Pratt in 1926, an attack regarded as angina pectoris with dyspnea by 1 observer might by another be called cardiac asthma with pain.

Clinical Features — The dominant clinical manifestation of left ventricular failure is pulmonary congestion and edema, which may vary in degree from scattered basal crepitations to gross waterlogging of the lungs and hydrothorax. The symptoms vary in severity from nocturnal cough and slight wheezing to severe dyspnea and asphyxia. As severe bronchial spasm is an inconstant feature of the attacks, the term "cardiac asthma" is not generally applicable. The clinical manifestations of left ventricular failure are grouped by Bedford as follows. (1) Paroxysmal pulmonary congestion; (2) pulmonary congestion of effort, and (3) chronic pulmonary congestion

1 Paroxysmal Pulmonary Congestion— I shall first describe an average kind of attack and then mention the common variations

A man in the sixties, perhaps known to have hypertension or to be subject to anginal pain, becomes increasingly short-winded, yet by avoiding physical effort manages to lead a fairly normal life. Tired after a rather strenuous day, or perhaps after dining not wisely but too well, he retires to bed and to sleep, to be wakened in an hour or 2 with a feeling of anxiety and of oppression in the chest He sits up, or even seeks the window, for more air; his heart is pounding, he starts to cough, and soon he is suffocating and fighting for breath.

Called from his bed, the doctor finds his patient a prey to distressing dyspnea, anxious, sweating, pale, and perhaps slightly cyanosed. The pulse is full and bounding, rate 120 or more, and regular. The blood pressure is high, especially the diastolic. The breathing may be noisy, either from bronchial spasm or from bubbling bronchial sounds.

The heart is enlarged to the left, and at the apex gallop rhythm is both palpable and audible. We shall also find signs of pulmonary hypertension, such as palpable systolic pulsation over the right ventricular conus and pulmonary artery, succeeded by a distinct shock as the pulmonary valves close.

The chest is hyper-resonant and emphysematous, bronchial spasm is likely, and there are basal crepitations. The cough, at first unproductive, is now associated with a little frothy sputum, perhaps slightly bloodstained, and, if we examine the handkerchief which the patient invariably clasps, we shall note the characteristic "salmon spots."

The cervical veins are either invisible or fluctuating with respiration. Examination of the legs and back reveals no trace of edema, but, if the attack has been a long one, or if it is not the first, the liver edge may be palpable.

Morphine is given, and after an hour or so our patient is more comfortable, and we can leave him till the morning. Then we find him much better, though still breathless on moving, and with a rather quick pulse rate. The blood pressure has fallen somewhat, though the diastolic level remains high, and, in taking it, we now have time to notice a definite alternation of the pulse.

There may still be râles and rhonchi in the chest, but in a few days' time, and after digitalis, the lungs become dry, and our patient is anxious to get about again

Minor attacks of pulmonary congestion cause nocturnal orthopnea and cough A patient may wake up once or more in the night with vague oppression in the chest, or with slight wheezing, quickly relieved by sitting upright, as often happens when those who use several pillows slip down in the bed during sleep. Another, not troubled unduly during the daytime, is liable to fits of coughing as soon as he lies down at night, with the result that his sleep is much disturbed. He may describe a curious tickling in the throat, due to laryngeal congestion or possibly of reflex origin.

In more severe forms the feeling of oppression in the chest at the start is often intense and may amount to acute pain Soon the whole chest is bubbling with fluid, and the patient becomes collapsed and cyanosed Profuse expectoration of pink frothy fluid is the rule, but there are exceptions, and I have not infrequently seen a patient, with grossly waterlogged lungs and deeply cyanosed, expectorate little or nothing This is the bronchoplegic form of attack described by Huchard-the coup de sang pulmonaire In this condition of circulatory collapse combined with severe asphyxia a semicomatose state may supervene, and whatever the blood pressure at the start it quickly falls, and the pulse becomes small After these severe attacks pulmonary edema may persist for days or weeks, and a transient hydrothorax is not uncommon

2 Pulmonary Congestion of Effort—In some patients paroxysmal dyspnea is provoked by effort or excitement during the daytime While hurrying, going uphill, or venturing out of doors from a warm room, they are pulled up suddenly by cough and dyspnea, which is not at once relieved by halting and continues until the chest is cleared by expectoration of bloodstained frothy sputum Gallavardın (1933, 1934) in particular has drawn attention to this kind of pulmonary edema, which occurs more commonly in patients with mitral stenosis, subject to paroxysmal dyspinea or pulmonary hemorrhage, than in left ventricular failure. Effort edema may be no more than a sudden aggravation of pre-existing pulmonary congestion, or it may occur in those whose lungs are usually dry. Gallavardin also describes pulmonary edema of effort in patients with angina pectoris and advanced coronary disease, at first they are pulled up by pain alone, but later, as the myocardium deteriorates, the effort pain is accompanied by dyspnea and bloodstained expectoration

3 Chronic Pulmonary Congestion— After an attack of nocturnal dyspnea the lungs may dry up quickly, or, if they do not, right-sided failure may follow, bringing some relief to the lungs There remains a group of cases in which pulmonary congestion persists, without appreciable systemic engorgement and with a normal venous pressure. In other patients chronic pulmonary congestion develops insidiously, without nocturnal paroxysms, and may persist for months or exceptionally for more than a year, without any signs of systemic congestion. They may suffer from some degree of nocturnal orthopnea and are hable to cough and hemoptysis, but because of the absence of systemic edema they are often thought to have bronchitis.

The effect of treatment must be admitted. Now that mercurial diuretics are regularly used in the treatment of pulmonary edema, many patients are probably kept systemically dry who would otherwise become dropsical; hence in them left-sided failure is artificially maintained. This is not necessarily so, for long ago Huchard described this chronic pulmonary edema, persisting for months or years and often mistaken for bronchitis.

Pulmonary congestion due to left ventricular failure may involve the pleura, and hydrothorax is by no means rare; it is usually left-sided, or if bilateral, larger on the left. Hydrothorax may quickly subside with rest and treatment, and will often be missed unless specially sought, or unless x-ray examination is promptly made.

In the early stages of left ventricular failure, pulmonary hypertension may be recognized on x-ray examination by an increase in the size and density of the arterial shadows in the lung roots, which remain sharply defined. There may be prominence of the pulmonary trunk, with the result that the heart becomes "mitralized," though this belongs rather to the later stages Immediately after an attack of acute pulmonary edema, the large dense hilar shadows are surrounded by a foggy zone, and only the peripheral lung fields remain clear. Pulmonary edema starts at the lung roots and later gravitates to the bases, hence,

x-ray evidence of pulmonary congestion precedes the clinical signs.

In left ventricular failure tachycardia is the rule, often preceding the onset of dyspnea. And at the onset of paroxysmal dyspnea the blood pressure often rises—with the diastolic pressure disproportionately high. Gallop rhythm was present in about half of Bedford's cases, and pulsus alternans in a third; both of which conditions are more common in hypertensive cases than in those with normal or low blood pressure. Almost invariably the cardiac rhythm is regular, apart from premature contractions. Paroxysmal auricular fibrillation occasionally occurs; and at times established fibrillation follows the attacks of dyspnea, but the onset of the typical syndrome of paroxysmal dyspnea never has been observed during the course of established fibrillation. The electrocardiogram is almost invariably abnormal in left ventricular failure in contrast to angina pectoris, in which the tracings are normal in about 40 per cent of cases. The commonest electrocardiographic pattern is left ventricular predominance combined with inversion of the T-wave in Lead I or in Leads I and II-which was found in 41 per cent of Bedford's cases in which electrocardiograms were taken Bundle branch block occurred in 17 per cent of the cases.

In isolated left ventricular failure the systemic circulation is little if at all affected, as proved by a normal or increased velocity of peripheral venous flow, a normal arteriovenous oxygen difference, and a normal venous pressure. In the pulmonary circulation, however, the presence of stasis is shown by diminished velocity of blood flow, a reduced vital capacity, and an increased blood content of the lungs. During a paroxysm of dyspnea the cardiac output is usually unchanged or decreased, but never in-

creased; and, if pulmonary edema becomes severe, the oxygen saturation of the arterial blood is lowered. The circulation time between arm and tongue, determined by the decholin method, is always increased in left-sided heart failure, usually it is well above 20 seconds (normal 10 to 17 seconds). (Decholin, a preparation of dihydrochloric acid, produces a sudden intensely bitter taste upon arrival in the mouth.—ED.) The arm-to-lung circulation time-measured by injecting 5 minims (0.3 cc) of ether into an antecubital vein and timing its arrival at the lung by the patient's perception of its odor-remains normal in the early stages of left-sided failure, but with gross pulmonary engorgement it may be prolonged. The normal ether time 1s 4 to 8 seconds By subtracting the ether (arm-to-lung) from the decholin time (arm-to-tongue) an index of the pulmonary circulation time (lung-totongue) is obtained, which is always prolonged in left ventricular failure (the normal being $4\frac{1}{2}$ to 10 seconds)

Diagnosis—"Once it is appreciated that, in conditions of left ventricular strain, pulmonary congestion may be the first and only objective sign of heart failure, diagnosis is rarely difficult. The onset of bronchitis or asthma for the first time in a man over 50 should at once suggest a careful scrutiny of the heart for evidence of hypertension, angina pectoris, and aortic disease. When, in such a case, cough and dyspnea are mainly nocturnal, especially if there is orthopnea or hemoptysis, a cardiac origin is likely Radiography is of great help, for it may disclose both cardiac enlargement and pulmonary congestion, and at the same time it permits the exclusion of intrathoracic neoplasm and chronic lung disease.

"Occasionally there is real difficulty in distinguishing between bronchial and cardiac asthma; if so, estimation of the arm-to-tongue circulation time by decholin will be decisive. In asthma and emphysema the arm-to-tongue time is normal or slightly shortened, but in paroxysmal cardiac dyspnea it is always prolonged during or near the paroxysm. The electrocardiogram is rarely normal in left ventricular failure, and it may provide objective evidence of myocardial disease when clinical signs are lacking."

Course and Prognosis - When pulmonary congestion is paroxysmal, prompt treatment may prevent or delay further paroxysms, but sooner or later they will recur, until eventually pulmonary congestion persists Right ventricular failure may follow a single severe attack of pulmonary edema or be delayed for months or years. As a rule, paroxysmal dyspnea ceases with the onset of failure of the right ventricle or of auricular fibrillation, but may return if systemic congestion is relieved by treatment. Not a few patients die suddenly, quite apart from the paroxysms, and others succumb to coronary thrombosis, or to a cerebral vascular accident. The average duration of life after the onset of paroxysmal dyspnea in the 96 fatal cases in Bedford's series was 122 months, a third of these died within 6 months, over half within a year, and 85 per cent within 2 years In 33 patients still living, the average duration of life to date is 20.8 months, which figure is unduly influenced by 2 patients who have lived 13 and 101/2 years, respectively The average duration of life in paroxysmal dyspnea is far shorter than in angina pectoris and slightly shorter than in coronary thrombosis. The prognosis in left ventricular failure is unquestionably influenced by treatment, and those live longest who receive prompt and adequate treatment at the start and continue under regular supervision

—The first step in the treatment of paroxysmal dyspnea should be directed toward diminishing the excitability of the respiratory center by the immediate administration of *morphine sulfate* in dosage of ½ grain (0.015 Gm.) hypo-

Treatment-Immediate Treatment

dermically. Atropine usually is administered along with morphine, but Bedford does not feel that this combination is superior to morphine alone. Morphine often is withheld in the presence of cyanosis or collapse, but these symptoms should not contraindicate its use. In Bedford's opinion adrenalin should never

be given, for it is as likely to do harm

as good

The next step in treatment is the relief of pulmonary congestion, which can most quickly be affected by venesection. Whenever there is gross edema of the lungs or much cyanosis, 15 to 20 ounces of blood should be removed by venesection. Venostasis, effected by the application of tourniquets or blood pressure armlets to the proximal ends of the limbs to reduce the venous return to the right heart, has been recommended as an alternative to venesection, but it appears clumsy and ineffective compared with venesection. In the average case of paroxysmal dyspnea oxygen inhalation is not required and often causes unnecessary alarm to the patient. The indication for oxygen is cyanosis, and then it should be administered continuously.

Later Treatment—As in all forms of heart failure, rest in bed is essential and must be of adequate duration. Bearing in mind the grave significance of paroxysmal dyspnea, at least a month's confinement to bed is not too long Digitalis in therapeutic dosage is of great value in paroxysmal dyspnea. Mercurial diuretics, combined with the usual restriction of fluid and salt intake, are most effective in dehydrating the lungs.

and increasing the vital capacity. Bedford tells of the dramatic effect of salyrgan in the case of a hypertensive patient who for 2 weeks had been tortured by nocturnal dyspnea without trace of systemic edema; and then after a profuse diuresis he slept peacefully at night for several months.

After nocturnal dyspnea is relieved, morphine may be replaced by an opiate given by mouth, and later a nightly dose of a barbituric acid derivative, such as luminal, will suffice. When the initial period of rest in bed is over, patients with left ventricular failure require careful supervision and should lead a much less active life. The evening meal should be light and a sedative always should be available. It is often wise to continue weekly injections of a mercurial diuretic for a time, or at least to reinstitute them as soon as moist sounds again appear in the lung bases. A few days in bed and a nightly opiate will often prevent the return of nocturnal dyspnea

Acute Pulmonary Edema

Positive Pressure Respiration in Treatment - In an experimental and clinical study of acute pulmonary edema. A. L. Barach, J. Martin and M. Eckman²² discuss its pathogenesis and the value of positive pressure respiration in treatment. The factors involved in the pathogenesis of acute edema of the lungs may be listed as follows: (1) Left ventricular failure; (2) increased permeability of the pulmonary capillaries; (3) (a) a persisting pathologically elevated negative pressure within the chest, or (b) an abrupt termination of expiratory effort and a consequent loss of the backward pressure on the pulmonary capillaries

In cases of respiratory obstruction the pathologically elevated negative pressure within the chest exerts a suction action

on the pulmonary capillaries, resulting in a tendency to ooze serum through their walls. Expiration against a constricted bronchial passage maintains a backward pressure against the pulmonary capillary wall, inhibiting the leakage of edema fluid. Therefore, in patients with pronounced asthma the use of morphine in doses which markedly diminish the respiratory effort has the danger of precipitating edema of the lungs. Also, the sudden development of pulmonary edema after aspiration of pleural effusion may be due at least in part to sudden removal of relative positive pressure and exposure of certain lung alveoli to resumption of negative pressure The expiratory grunt in lobar pneumonia has the physiological advantage of maintaining increased positive pressure against the alveolar capillaries at the beginning of expiration, thus preventing pulmonary edema And patients with emphysema frequently partially close their lips during expiration and find that their breathing is much easier than when the mouth is open. In the treatment of patients with chronic asthma of moderate degree, increased resistance to the egress of air during expiration by this procedure for 3 to 5 minutes often may terminate an attack of wheezing, indicating that the backward distending pressure on the bronchioles tends to keep them patent.

In 8 clinical cases inhalation of **helium** and oxygen, or oxygen alone, under positive pressure applied continuously throughout the respiratory cycle (which method has been described in detail by A L Barach²³) effected a swift clearance of edema and a betterment of the state of circulation. The positive pressure was achieved by means of a closed circuit apparatus in which the ventilation and pressure are produced by a motor blower unit capable of maintaining a pressure

as high as 10 cm. of water; a hood, making closure at the neck, modeled after the Benedict helmet metabolism apparatus, was employed Positive pressure decreases the amount of blood entering the right heart, and in that way diminishes pulmonary congestion and facilitates the clearing of pulmonary edema. When the lungs are distended from without by positive pressure, there are the additional effects: (a) Lowering of the negative pressure within the chest during inspiration; and (b) a direct opposing physical pressure on the pulmonary capillaries, especially during expiration. When pulmonary edema is due to irritation and inflammation, resulting from an increased permeability of the pulmonary capillary walls, positive pressure respiration is at times less effective in clearing the signs of edema.

Auricular Fibrillation and Flutter

Treatment - Administration of Digitalis—G Fahr24 states that at present digitalis is standardized according to the U S P XI so that 10 minims (0.65 cc) of the tincture or 1 grain (0065 (m) of the powdered leaf is 1 Hatcher-Brody cat unit, whereas in the previous editions of the U S Pharmacopeia 15 minims (1 cc.) of tincture or 1½ grains (01 Gm) of the powdered leaf contained 1 cat unit. In other words, 11/3 grains (01 Gm.) of the standard U.S. P XI powder is equivalent to 16 Hatcher-Brody cat unit. One cat unit of U. S P XI powdered leaf to each 10 pounds (45 kg) of body weight when fixed in the body gives very nearly the optimal effect in lowering the ventricular rate in auricular fibrillation As a rule, that amount is perfectly safe And if it should not bring about the desired therapeutic effect, from 10 to 30 per cent increase in dosage usually will. If toxic manifestations occur, administration of the drug should be discontinued for from 24 to 72 hours.

Certain individuals are sensitive to digitalis, and therefore reduction of the ventricular rate may be difficult because of the incidence of nausea, vomiting and extrasystoles. The appearance of coupled beats during the course of digitalis treatment is a toxic manifestation calling for immediate discontinuance of the drug until the extrasystoles disappear. The ventricular rate should never be reduced below 60 per minute, since a rate below that level decreases the efficiency of the heart action. A small number of adult patients, usually those with coronary artery disease or with other disease which reduces conduction through the bundle of His, will require less than the calculated optimum dose. Such individuals frequently show apical rates of 100 or less per minute before any digitalis has been given. In hyperthyroidism, digitalis usually fails to lower the ventricular rate; in such event a compound solution of iodine should be administered, and surgical operation should be performed when safe After thyroidectomy, auricular fibrillation disappears in more than 50 per cent of the cases. In toxic conditions associated with fever, caution should be exercised in the administration of digitalis

After the stage of optimum digitalis effect has been attained, a daily dose of 1 cat unit is necessary to maintain the benefit, since approximately that amount of digitalis is removed from the body each day. Doses of digitalis of this size do not reduce the volume flow through the coronary arteries nor injure the myocardium. In fact, 1 cat unit a day may be given to a 150-pound (68 kg.) patient for years without danger. If vomiting necessitates rectal administration, similar dosage may be given as in the case of oral administration. (Since administration of

digitalis by rectum is apt to prove irritating, intravenous or intramuscular injection is preferred by most clinicians when the patient is unable to take the drug by mouth because of vomiting, coma or inability to swallow.—ED.)

In myocardial failure of moderate degree, 7 days may be taken to bring about optimum digitalization. In such event 21 cat units are necessary for a patient weighing 150 pounds (68 kg.)—15 cat units being necessary for the optimal amount to be fixed in the body and 6 cat units being required to replenish the loss of digitalis during the 6 days following the day on which the drug is first given. If the ventricular rate is above 70 per minute on the patient's return (resting quietly in the examining room), 2 cat units are given daily until the heart rate is between 60 and 70 per minute. After the latter rate has been attained, 1 cat unit is given each day. In dispensary practice the calculated optimum amount often is given within a shorter period if the degree of failure is quite severe. For example, 17 cat units may be given to a patient weighing 150 pounds (68 kg.) over a 3-day period; and on the patient's return on the third day 1 or 2 cat units are prescribed daily for the next 3 days depending upon whether the ventricular rate is close to 60 or 70, or is higher.

In hospital practice 15 cat units usually are given to a 150-pound (68 kg) patient within the first 32 hours, one-third of the calculated amount being given at once and one-sixth every 8 hours for 4 doses. Thereafter a daily dose of 1 or 2 cat units is administered depending upon the ventricular rate (Before prescribing large doses of digitalis it is important to make certain as to whether or not any digitalis preparation has been taken during the 2 weeks immediately preceding, in order that the size of the dose may be regulated accordingly—ED) In

case of overwhelming heart failure with auricular fibrillation and a high ventricular rate of 150 to 200 per minute, the drug is administered intravenously. In Fahr's opinion preparations of digitalis lanata are good for this purpose, although ampoules of well-known preparations, such as digalen or digifolin, or even tincture of digitalis diluted with saline solution, may be used. Eight cat units of digitalis purpurea may be given safely at 1 intravenous injection to a patient weighing 150 pounds (68 kg.), which dosage is equivalent to 1 milligram of digilanid C or 1 milligram of digoxin (preparations of digitalis lanata).

Potency of Digitalis Preparations of 1936 Pharmacopcia—In a paper dealing with the potency of digitalis preparations of the Pharmacopeia of 1936 (eleventh revision), C. W. Edmunds²⁵ explains that U. S P. XI digitalis is from 25 to 30 per cent stronger than the digitalis of the 1926 U.S. P. X, and that statements to the effect that the strength of digitalis preparations has been increased 50 to 70 per cent, as expressed by G Fahr^{24, 26} and other investigators, are erroneous-being based in most, if not all, instances on faulty assay technic or calculations. To convert U S P. digitalis (frog) units into cat units is not safe, because there has not been sufficient study of the relationship between the results obtained by the 2 methods; and, furthermore, the fact must be recognized that 0.744 Gm of the U S P XI reference or standard powder²⁷ is equivalent in potency to 1 Gm of the international powder The increase in strength has arisen from the fact that the international standard digitalis powder has been adopted as the standard for the United States in order to secure, as far as possible, international uniformity in the potency of the drug. The increase in the potency of the official

preparations must be taken into consideration by the physician, especially when inducing rapid digitalization by the administration of large doses at relatively short intervals. It is also well for the physician to advise each patient to adhere to the use of a certain brand of digitalis.

Administration of Quinidine — In the treatment of auricular fibrillation not associated with serious organic heart disease, quinidine is the drug of choice. Such attacks may be precipitated by severe physical exertion, great excitement or emotion, drinking bouts, infectious disease, drugs, and chemicals. The outlook in these cases usually is excellent; but occasionally heart failure will develop even though there is no evidence of organic heart disease. As a rule, normal rhythm can be restored by the use of quinidine.

Many competent cardiologists warn against the use or over-emphasize the dangers of quinidine in the treatment of auricular fibrillation accompanied by organic disease of the heart. As the drug exerts a toxic action on the heart muscle, it cannot be denied that there are grave dangers inherent in its use Because of the fact that quinidine decreases the strength of the contraction of the heart muscle, its use in cases of auricular fibrillation complicated with serious organic heart disease or myocardial failure must be preceded by thorough digitalization of the heart. The ventricular rate should be reduced by the administration of digitalis to about 60 or 70 per minute for a period of approximately 2 weeks before instituting quinidine therapy. In cases with severe myocardial failure a longer period should be allowed to elapse before administration of quinidine The commonest toxic manifestations of quinidine are epigastric distress, nausea, vomiting, headache, diarrhea, ringing in

the ears, palpitation and apprehension. Embolism is a danger which at times occurs; other dangers, rarely encountered, are asystole, syncope, and epileptiform convulsions. When evidence of digitalis poisoning is presented, quinidine should not be given in doses larger than 15 grains (1.0 Gm.) a day because of the danger of serious summation of the toxic effects of both drugs.

A trial of quinidine is recommended by Fahr in cases of mitral stenosis with auricular fibrillation in which the total transverse diameter of the heart is not enlarged more than 20 per cent, and when the abnormal rhythm has not been present for more than 6 months. these cases the use of auinidine must be preceded by digitalization, and circulatory efficiency should be restored for 2 weeks before beginning quinidine therapy. It has been demonstrated by A. C. Kerkhof²⁸ and other investigators that the efficiency of the heart is increased 25 per cent in mitral stenosis with auricular fibrillation when regular beating of the auricles is restored, even though the heart has been kept at an optimum rate by the use of digitalis during the period of fibrillation Quinidine therapy may be attended by benefit also in auricular fibrillation associated with hypertensive heart disease and coronary arteriosclerosis.

(In the experience of Maurice Campbell and F. W. Gordon²⁹ in fibrillation without mitral stenosis or goiter "aftertreatment is not generally needed for more than 3 months, but if relapse occurs on omitting quinidine, a second course should be given, and, if successful, quinidine should be continued for longer

. The case is not suitable (for quindline therapy) if there has been gross congestive failure or if any signs of failure persist after treatment with rest and digitalis, or if the heart is greatly

enlarged (more than 14.0 cm. maximum transverse diameter in a patient of about 10 stone), or if fibrillation has been established for 6 months. The presence of any 1 of these 3 usually means that treatment with digitalis should be preferred. In intermediate cases the decision will be made according to how nearly they fall into 1 or other of these groups. When there is mitral stenosis. these conditions must be strictly observed. Least attention need be paid to them if fibrillation is due to goiter, as, if necessary, partial thyroidectomy will convert an unfavorable case into one favorable for quinidine."—ED.)

Quinidine in 2 or 3 grain (0.13 or 0.2 Gm) tablets is administered by Fahr, as follows. One tablet is given on the first day to test for idiosyncrasy to the drug; the next morning 1 tablet is given at 8 and another at 9 o'clock; on the third day 1 tablet is given at 8, another at 9, and another at 10 A M The dosage is increased 1 tablet a day, all the tablets being given at 8, 9 and 10 a m. (Many cardiologists prefer giving quinidine in dosage of 6 grains (04 Gm.) every 4 hours throughout the 24-hour period, with omission of 1 period during the night -ED) A total of 36 grains (23 Gm) a day may be given; but the inexperienced physician should stop at a daily dose of 24 grains (15 Gm), with which regular rhythm will be restored in at least 50 per cent of all cases. After the restoration of normal rhythm, 9 grams (06 Gm) should be prescribed daily as long as possible for its maintenance; and if rather severe invocardial failure was present before beginning digitalis therapy, I cat unit of digitalis should be given daily in addition to the 9 grains (06 Gm) of quimdine During the treatment the patient should be in a hospital or at home with a nurse to observe the pulse and general

condition until the pulse becomes regular.

In auricular flutter in which the ventricular rate is between 130 and 160 beats a minute (due to 2:1 heart block -which as a rule is present) the ventricular rate usually can be reduced by administration of digitalis in therapeutic doses. Such treatment usually brings about 3:1 or 4:1 block, the rate becoming somewhat irregular due to a shifting from 1 type of block to the other, the optimum ventricular rate being between 60 and 70 per minute; and in about 90 per cent of cases the auricular flutter will change to auricular fibrillation if this state of digitalization is kept up for a week or 2. In cases in which fibrillation does not develop after digitalization and in those in which fibrillation is not followed by regular rhythm after digitalis has been discontinued, the use of quinidine is advisable. The percentage of success in bringing about return of normal cardiac mechanism with quinidine is no greater in auricular flutter than in fibrillation. When the condition remains refractory, it is necessary to continue with digitalis therapy in order to block the conduction between the auricles and ventricles. When other methods fail, acetyl-beta-methylcholine (mecholyl) in doses of $\frac{1}{2}$ to $\frac{5}{6}$ grain (30 to 50 mg) subcutaneously —as recommended by I. Starr, Ir 30 will occasionally restore regular sinus rhythm.

Extrasystoles

Serious organic heart disease is not present in most cases of extrasystoles (premature beats). Unless their incidence is greater than 12 per minute, the efficiency of the heart is not adversely affected. Extrasystoles not associated with organic heart disease usually are found in nervous, worried or apprehensive individuals. The patient usually does

not suffer from symptoms of cardiac failure, but is merely embarrassed and frightened by the "skipping" or "palpitation." Treatment in these cases requires first of all reassurance that the condition is not serious; worry and undue fatigue must be removed; tobacco or coffee must be prohibited; sedatives, such as bromides, barbiturates or codeine, may be necessary to reduce excitability; and a change of environment is often useful. Frequently extrasystoles are associated with flatulence, which at times can be relieved by lying on the left side with subsequent disappearance of the extrasystoles. When these measures fail, quinidine, either alone or with strychnine ($\frac{1}{3}$) grain—2 mg), 3 times a day, frequently will abolish the irregularity. Quinidine should be given in doses of 3 grains (02 Gm), 3 times a day, increasing to 4 times a day, or even to 4 grains (0.26 Gm.), 3 times a day.

Extrasystoles are found in at least 10 per cent of all cases of coronary thrombosis, in which condition they are of grave significance and quinidine must be given (in doses of 3 grains—0 2 Gm —every 2 or 3 hours for 3 or 4 doses) to prevent the appearance of ventricular tachycardia If the extrasystoles disappear, quinidine may be repeated after 6 to 8 hours to prevent recurrence As digitalis predisposes to the incidence of extrasystoles and ventricular tachycardia in coronary thrombosis, it should not be administered unless auricular fibrillation or flutter with ventricular rate above 95 or moderately severe myocardial failure is present

Paroxysmal Tachycardia

Treatment—An attack of paroxysmal tachycardia may have serious consequences in a patient with advanced cardiac disease. Fahr has had more success in preventing auricular or auriculoven-

tricular nodal paroxysmal tachycardia with digitalis than with quinidine. In treatment of an attack, an ice bag over the precordium proves of advantage. And pressure on the carotid sinus, effected by placing the second and third fingers over the carotid artery at the level of the thyroid cartilage and pressing the artery very firmly back against the transverse process of the cervical vertebra, occasionally stops an attack. This should be tried first on the right carotid and then on the left, and if it does not prove successful, pressure on the eyeballs may be tried. Sometimes the patient can stop an attack by taking a deep inspiration, closing the glottis, and attempting to exhale forcibly. A feather, or tongue depressor pressed or rubbed against the posterior pharynx as to provoke vomiting also will occasionally terminate an attack. The administration of from 1 to 2 drams (3.8 to 7.5 cc.) of fresh syrup of ipecac to cause nausea and vomiting-as recommended by S. Weiss and H. B. Sprague³¹—often proves efficacious; and if the desired effect is not obtained after 45 minutes, the dose may be repeated or slightly increased One-third ounce (10 cc) of digalen or digifolin administered intravenously in 1 or 2 doses to a patient weighing 150 pounds (68 kg) also may prove successful in terminating atacks

Acetyl-beta-methylcholine chloride (mecholyl) is probably the most certain of all drugs in the termination of attacks of paroxysmal tachycardia of auricular or auriculoventricular nodal origin. The drug is a powerful stimulator of the vagus nerve, and should not be used when there is a tendency to asthma. It produces sweating, voniting, and vaso-dilatation, and occasionally substernal pain and defecation. A dose of ½ grain (20 mg.) is recommended for younger patients, and ½ grain (30 mg.) for older individuals. When the drug is adminis-

tered subcutaneously, the patient should be lying down, since fainting may occur if sitting. If the attack does not stop in 2 or 3 minutes, the dose is repeated. In the experience of Starr,³⁰ the drug effect had to be supplemented with *carotid* sinus pressure in 20 per cent of the patients.

Ventricular paroxysmal tachycardia is found most frequently in patients with coronary artery disease. It is not at all infrequent in coronary thrombosis, and may be the precursor of ventricular fibrillation and death. Since digitalis increases the tendency to ventricular paroxysmal tachycardia (and probably to ventricular fibrillation), it should not be given in coronary artery thrombosis when that type of tachycardia is present. Quinidine should be administered: 3 grains (0.2 Gm.) should be given by mouth first to test the patient for idiosyncrasy to the drug, and then if no untoward manifestations appear, 6 grains (0.4 Gm.) should be given an hour later; and if the tachycardia has not ceased by that time, it is well to wait 4 hours before repeating it, since the maximal effect on ventricular rate comes 4 hours after administration of the drug by mouth, and most attacks of ventricular tachycardia will cease with a total of 15 grains (1 Gm.) administered in this manner Fahr states that he has never failed to stop ventricular tachycardia with quinidine (In a discussion of Fahr's paper, Dr. W. S Kerr, of San Francisco, spoke against the routine use of quinidine in paroxysmal ventricular tachycardia, on the ground that in a high percentage of cases there is present a serious vascular disease of the heart with block in the conduction system, and that since quinidine acts on the conduction system, tending to increase the degree of block, as well as on the muscle, the dangers of making the patient worse and

producing ventricular fibrillation are considerable.—ED.)

Heart Block

Treatment-In cases of partial auriculoventricular heart block, atropine sulfate in doses of $\frac{1}{100}$ grain (0.6 mg.) will reduce sufficiently the block in the bundle of His that digitalis in moderate doses may be administered safely to increase myocardial efficiency. In complete auriculoventricular heart block, digitalis may be given without fear of reduction in ventricular rate. Epinephrine in dosage of 5 to 10 minims (0.32 to 0.65 cc.), every 1 or 2 hours if necessary, subcutaneously is most valuable in the prevention of the Adams-Stokes syndrome. At the time of asystole, there is no blood flow, and if asystole with syncope and convulsions last from 30 to 60 seconds. epinephrine, 3 to 5 minims (02 to 0.3 cc.), must be given intracardially by injection in the fourth left interspace just lateral to the sternal border. Ephedrine hydrochloride in dosage of 3/4 grain (0048 Gm), 4 to 6 times a day, also is of value in the presence of attacks of Adams-Stokes syndrome. (The action of ephedrine is more gradual and prolonged than that of epinephrine—ED.) In electrocardiogram should be taken to determine whether the Adams-Stokes seizures might be due to runs of ventricular fibrillation or of frustrate extrasystole. In such event, neither epinephrine nor ephedrine should be given since these drugs only increase this tendency, but rather the use of quinidine is indicated The treatment of heart block is the least satisfactory treatment of any of the arrhythmias

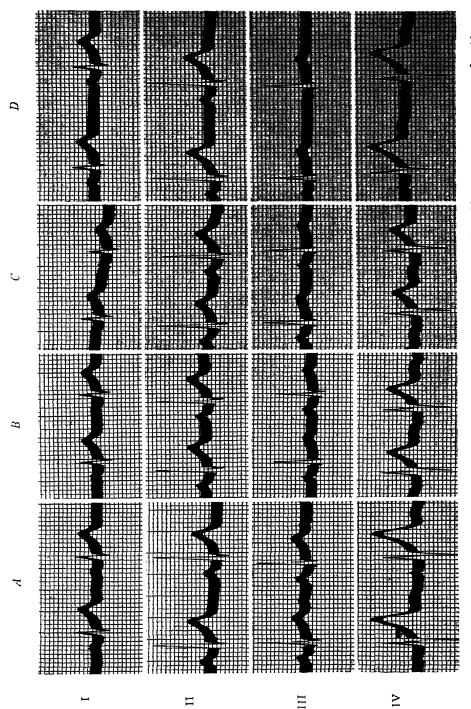
Electrocardiography

Electrocardiographic Changes Caused by Induced Anoxemiaasa Test of Coronary Insufficiency—In search

of an objective test for the detection of coronary artery insufficiency, changes in the form of the electrocardiogram following the induction of generalized anoxemia have been studied by R. L. Levy, H. G. Bruenn and N. G. Russell, Jr.,32 in 105 persons (comprising 66 normals, 23 with disease of the coronary arteries, 11 in whom cardiac disease was suspected but doubtful, and 5 with severe anemia). The apparatus used enabled the subject to breathe a mixture of 10 per cent oxygen and 90 per cent nitrogen at the normal rate of pulmonary ventilation, without rebreathing. A tank containing 100 per cent oxygen was in the circuit, so that if necessary, by turning a needle valve, anoxemia could be quickly relieved. Observations were made at least 2 hours after the last meal; the usual period of observation was 20 minutes; and a control 4-lead electrocardiogram was made, with the apparatus in place before beginning the test, and additional tracings were taken at the end of 5, 10, 15, and 20 minutes, as well as after 100 per cent nitrogen had been given for approximately 1 minute, or until cyanosis was abolished.

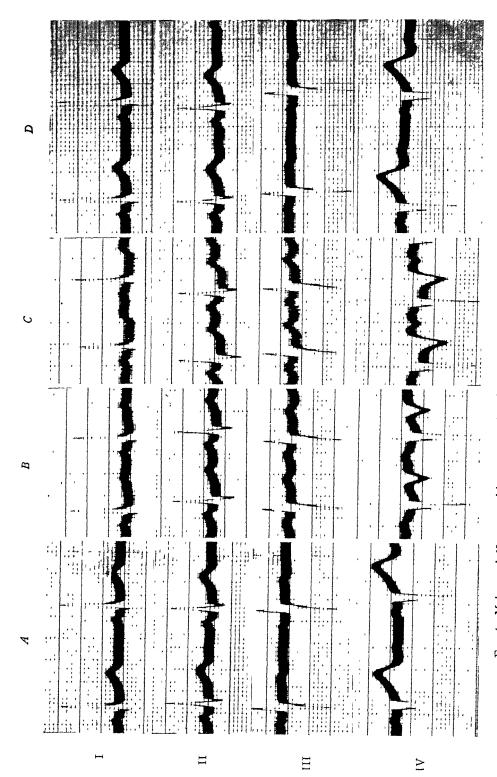
All of the patients became distinctly cyanotic while breathing 10 per cent oxygen None of the normal individuals and none of those with anemia experienced pain during anoxemia Of 17 patients with coronary sclerosis and spontaneous attacks of pain, all showed abnormal electrocardiographic response to the tests; 12 complained of pain after varying periods, which was relieved promptly by inhalation of 100 per cent oxygen. In 6 patients with previous coronary occlusions and healed myocardial infarcts, the test yielded negative results; 1 complained of pain and 1 of mild substernal pressure during the period of anoxemia The absence of changes in the form of the electrocardiograms of these 6 patients may be regarded as indicating that the remaining coronary arteries were able to maintain an adequate flow of blood through the myocardium—in view of the fact that they were clinically well. In 11 patients with suspected but doubtful

coronary artery disease, the test was negative—confirming the clinical impression that discomfort was not of cardiac origin. In the 5 patients with marked anemia but without signs of cardiac disease, significant changes in the T-waves.



B, After breathing Control. male technician, aged 29 years. minutes, D, After 1 minute of slightly Am J 1

comparable to those seen in the presence of coronary sclerosis, occurred in every instance. Anoxemia added to severe anemia brought about the same result, in this respect, as when added to ischemia; but pain was conspicuously absent, and also



toon negative A, Control, a normal record B, After 5 minutes of 10 per cent oxygen C, After 8 minutes; complained of pain, test stopped D, After 1 minute of 100 per cent oxygen T_1 and T_4 reversed their direction RS-T junction depressed in all leads In D, reversion to the form seen in A (Levy, Bruenn and Russell: Am J, M Sc) Fig 4-Male, aged 69 years, with coronary sclerosis and attacks of anginal pain for 5 years Physical examina-

in no case were the RS-T junctions displaced more than 1 millimeter.

On the basis of 700 electrocardiograms taken during 112 tests, the following tentative criteria for normal and abnormal responses have been evolved:

Normal—1. The RS-T junction is not displaced more than 1 mm in any lead.

- 2. The T waves tend to decrease in amplitude.
- 3. Partial or complete reversal of the direction of T in Lead I or Lead IV F, or both, in the absence of any RS-T displacement in these leads, is of uncertain significance. It was observed in 2 of 66 supposedly normal persons.
- 4. Partial or complete reversal of the direction of T in Lead II or Lead III, or both, even though associated with RS-T displacement of less than 1 mm., is of no significance. It was observed in 22 of 66 supposedly normal persons (see Fig. 3).

Abnormal—1 A change in the level of the RS-T junction of more than 1 mm in any lead, even though unassociated with changes in the T waves, is abnormal. Its importance is increased if combined with partial or complete reversal in the direction of T in Leads I or IV F, or both

- 2 Partial or complete reversal in the direction of T in Lead I is abnormal when associated with any displacement of the RS-T junction in this lead. Such displacement may be as little as 0.5 mm
- 3 Complete reversal in the direction of T in Lead IV F is always abnormal
- 4 Partial reversal of the direction of T in Lead IVF, associated with any displacement of the RS-T junction in this lead, is abnormal Such RS-T displacement may be as little as 0.5 mm (see Fig. 4).

The level of oxygen saturation of the blood was variable. But there was no direct relationship between the degree of anoxemia and the magnitude of the changes seen in the electrocardiograms, nor did the duration of the test determine the extent of such changes For example, in certain patients complaining of pain at the end of 4 minutes, the changes at this time were striking. Although alterations in the electrocardiograms appeared quickly, they tended to regress gradually;

even after 100 per cent oxygen had been breathed for a minute, the return to the form of the control record was usually incomplete. No serious untoward effects occurred. But because of 2 unpleasant reactions, it is suggested that the test should not be given to patients with cardiac insufficiency, and should not be repeated in the same individual within 24 hours. In a woman, aged 60 years, with symptoms of early cardiac insufficiency, on whom the test was performed twice within an hour, mild pulmonary edema occurred after the second period of anoxemia. And in a male, aged 56 years, with a history of dyspnea as well as pain and an electrocardiogram showing bundle branch block, there developed nonproductive cough, scattered râles in the lungs and slight substernal pain after breathing 10 per cent oxygen for 7 minutes. Prompt relief was afforded by the inhalation of 100 per cent oxygen.

These studies suggest that changes in the form of the electrocardiogram occasioned by induced anoxemia may be used as a clinical test for insufficiency of the coronary circulation, whether this be manifest or latent. An index is afforded of the adequacy of the "coronary reserve." The test should be of value in distinguishing pain of coronary origin from pain in the chest due to other causes, as well as from pain referred from the abdomen Also it is possible that it can be employed to study the effect of drugs and various surgical procedures on the efficiency of the coronary blood flow.

In a previous study, in which a similar breathing apparatus was employed with 12 per cent oxygen and 88 per cent nitrogen, which reduced the oxygen saturation of the arterial blood to a level ranging from 67 to 83 per cent, R. L. Levy, A. L. Barach and H. G. Bruenn³³ concluded that cardiac pain induced by in-

duction of systemic oxygen want is not a reliable index for the detection of coronary insufficiency, partly because it represents a subjective end point, and also because so many complex factors are concerned in its production. In none of 11 patients without cardiac disease did pain occur; and in 37 patients with heart disease there was no constant relationship between the occurrence of cardiac pain and changes in heart rate, respiratory rate, blood pressure, venous pressure, circulation time, and the degree of arterial unsaturation. Pain occurred inconstantly in repeated tests, except in 2 patients with aortic stenosis and in 1 with advanced coronary disease; and in 2 patients with healed infarcts of the heart untoward effects were observed, but both recovered promptly. The latter observations point out the danger of aeroplane flights for persons with disease of the coronary arteries, as an oxygen concentration of 12 per cent is equivalent approximately to an altitude of 15,000 feet The study showed that oxygen want is an important and apparently the determining factor in the causation of cardiac pain, and is most effective when the coronary blood flow is reduced, and that ischemia and anoxemia complement each other synergistically as pain-inducing agents in the heart, although neither is wholly effective alone. In the incidence of pain, of particular importance is the emotional status of the patient, as well as his usual ability to appreciate painful sensations; and other variables are the degree of sensitivity of the afferent nerve endings in the heart, the state of the nerve pathways which conduct pain impulses from the heart to the central nervous system, the total metabolism of the patient and the oxygen-carrying capacity of the blood. The authors concluded that the induction of systemic oxygen want may prove to be useful as

a test for coronary insufficiency, but for general use at this time it is not to be recommended.

Electrocardiographic Changes Occurring with Alterations of Posture—Definite changes in the appearance of the Q-R-S and T-waves of the electrocardiogram on alteration of the posture from the dorsal recumbent to standing or sitting positions were observed by L. H. Sigler³⁴ in a study of 100 cases. The changes in the T-waves usually occurred independently or were different from those expected from the preceding Q-R-S complexes. In some cases, the changes were so marked as to make the electrocardiogram appear abnormal. The changes in the T-waves consisted of diminished voltage, flattening, or actual conversion from a positive to a negative phase in 1 or more leads—usually occurring in the third lead or in the third and second leads (Fig 5) The changes occurred as frequently in normal as in diseased hearts. In normal hearts there was a greater tendency for the electrical axis of the Q-R-S complex to shift to the right and of the T-wave to the left, while in the diseased heart the tendency was of shifting to the left for the Q-R-S and to the right for the T-wave. In most cases the changes did not conform to the theory of the Einthoven equilateral triangle, for the shift in the electrical axis was not always as predicted from the supposed shift of the anatomical axis. The phenomenon may be explained on the theory that on alteration of body posture there occurs a change in contact of the adjacent conducting media with different portions of the heart, producing a variation in conduction

In a group of 16 individuals, including normal subjects and patients with heart disease, the variations in the form of chest leads with change in posture have been studied by H. J Stewart and R. L. Bailey.³⁵ The changes consisted chiefly of a decrease in the amplitude of the R- and T- waves, which varied concordantly, and, in many instances, a decrease in the amplitude of the S-waves, as the subject's posture was changed from supine, to sitting, to lying on the left side. In several cases, positive T-waves became diphasic, and diphasic T-waves became negative. The changes were more marked when the exploring

was admitted to the hospital complaining of difficult breathing and cramping pains in the abdomen and extremities. An examination showed deep and rapid breathing and the typical carpopedal spasm of tetany, but revealed no abnormality of the heart or lungs. An electrocardiogram, however, showed pronounced flattening of the T-waves. When the patient was reassured and persuaded to breathe normally, the symptoms rapidly

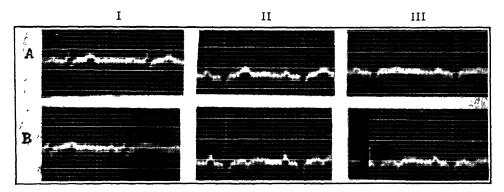


Fig 5—Changes in the T-wave in Leads II and III on change in posture. No appreciable changes in the Q-R-S complexes. A, Recumbent; B, standing The electrocardiogram was obtained from a normal heart (Sigler · Am Heart J.)

electrode was placed at the apex than when in the midsternal line at the level of the fourth intercostal space or halfway between this point and the apex. In every case the indifferent electrode was placed in the interscapular region. Since in certain cases the change was sufficient to confuse or alter the interpretation of the electrocardiogram, account must be taken of the posture of the patient in the interpretation of precordial leads.

Effects of Alkalosis and of Acidosis Upon the Human Electrocardiogram—The finding of pronounced flattening of the T-waves in a 23-year-old male medical student with hysterical overventilation and tetany prompted an experimental investigation of the effects of alkalosis and acidosis on the human electrocardiogram by P. S. Barker, E. L. Shrader and E. Ronzoni 36. The patient

disappeared and on the following day his electrocardiogram was normal

In 13 experiments made by Barker and his coworkers on 4 normal voung adults in whom well-developed tetany was produced by voluntary overbreathing, the T-waves of Lead I became much smaller during the overbreathing, and in 10 instances T of Lead II became smaller. In 2 instances, T of Leads II and III became slightly taller, while in 5 other experiments T of Lead III became taller In nearly all of the experiments, the R-waves became smaller in Lead I and taller in Lead III In these experiments blood samples from the arm veins showed alkalosis - with a hydrogen-ion concentration of 7.46 to 7.65 — at the height of the tetany.

In 7 experiments on 4 subjects, in which moderate alkalosis was produced

by the administration of sodium bicarbonate in single doses of 375 to 750 grains (25 to 50 Gm.) by mouth, electrocardiographic changes usually were apparent within 2 or 3 hours, and were most pronounced 5 or 6 hours after the ingestion of sodium bicarbonate. In 5 of the 7 experiments, the alkalosis was accompanied by a definite reduction in the

became much taller immediately after the exercise, taller in all 3 leads in 3 experiments, and in in Leads I and II in the other. The T-waves returned to approximately normal within 5 to 10 minutes after the exercise, and in 2 experiments they were slightly smaller than normal from 10 to 15 minutes after the exercise while the venous blood still

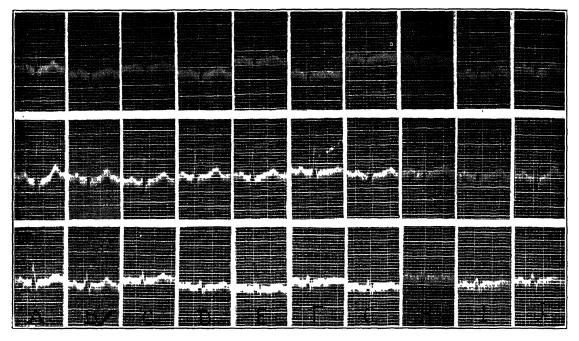


Fig 6—Experiment 28, subject A A, Control B to I, Curves taken at hourly intervals following the ingestion of 50 Gm of sodium bicarbonate J, Twenty-six hours later. The pH of the venous blood rose to 758, and the CO2 combining power to 748 vol. per cent. (Barker, Shruder and Ronzoni. Am. Heart J.)

amplitude of the T-waves of the electrocardiograms in Leads I and II or in all 3 leads (Fig. 6). The electrocardiographic changes were not directly proportional to the degree of alkalosis.

Definite acidosis was produced in 4 subjects by exercise, consisting of running up and down stairs until shortness of breath and fatigue were quite pronounced. The hydrogen-ion concentration of the venous blood fell to between 7.12 and 7.18, and returned to approximately normal within 15 to 30 minutes. In the electrocardiograms, the T-waves

showed evidence of acidosis. The R-waves changed but little The heart rate did not return to normal for 20 to 30 minutes after the exercise

Exercise of similar degree performed after large doses of sodium bicarbonate was followed by shortness of breath and fatigue of about the same degree as following exercise alone. Mild acidosis produced by the ingestion of single large doses of ammonium chloride, 225 to 375 grains (15 to 35 Gm.), caused the T-waves to become taller in all 3 leads

Since pronounced degrees of acidosis and alkalosis are relatively uncommon, the clinical application of these observations is probably quite limited. However, they may offer an explanation for occasional electrocardiographic changes not otherwise understood.

Electrocardiographic Changes Induced by Taking Food - Changes in the electrocardiogram in 7 of 9 normal. healthy, young adults following an ordinary mixed meal have been reported by M. Gardberg and J. Olsen.³⁷ Tracings were taken before, and again within 30 minutes after the meal. The changes consisted of a 30 to 50 per cent decrease in the height of the T-waves in Lead I or III, or in all 3 leads. In 1 case, T₁ was not only markedly lowered but became notched also; and in another case T₃, which was previously upright, became inverted. The electrocardiographic changes were not related to change in the heart rate. The change does not reach its maximum until 1 hour after the food is taken, and persists at this level for 11/3 to 2 hours. In no case did sufficient change in the electrical axis occur to explain the alterations in the height of the T-waves

Subacute Bacterial Endocarditis

For many years subacute bacterial endocarditis has been considered practically incurable. That perhaps the time has come to change this conventional outlook is emphasized by J. A. Capps³⁸ in a study of 139 cases, 11 of whom were living from 8 to 26 years after the onset of infection. It is possible that too much attention has been focused upon the septic type of the disease, which nearly always has a fatal outcome, and that a group of patients with a mild degree of infection in which there is a chance of recovery has been overlooked. In Capps' article the progress of our knowledge of

the disease from its earliest discovery in 1855 to our present-day conceptions, and the criteria for diagnosis are reviewed; and attention is called to variation in the incidence of disease from year to year, and to the importance of early recognition of mild cases and of prolonged rest in treatment.

Streptococcus viridans commonly inhabits the throat, tonsils, sinuses, teeth, and intestinal tract, and less frequently the gall-bladder, bronchi, urinary bladder and genital organs. And a patient with an old rheumatic heart valve or a congenital heart lesion is peculiarly vulnerable to subacute bacterial endocarditis. The incidence of the disease varies year after year. Few cases were observed by Capps from 1910 to 1920; there was an abrupt rise in the number of cases in 1922 (12 cases), which reached a peak in 1923 (22 cases); a decrease was observed in the following year (13 cases); and then an irregular number of cases was observed from 1925 to 1937. The experience at the Massachusetts General Hospital from 1910 to 1926 is comparable: from 1910 to 1921 there occurred from 2 to 8 cases a year; in 1922 the number increased to 9, and in 1923 to 16: in 1924 it fell to 8: in 1925 it rose to 14; and in 1926 the number was down again to 7 cases. Eight of the 11 cases of recovery reported by Capps occurred in the period from 1920 to 1924; no instance of recovery has been seen since 1924 An interesting fact is that 9 cases with recovery reported by E. Libman (Tr A Am. Physicians 48 44, 1933) occurred in the period from 1921 to 1924, and that he records no recoveries since 1924. The patients now considered as recovered with few exceptions were up and around when first seen, complaining of loss of weight and appetite, fatigue, palpitation and sweating; they were in marked contrast to the septic

appearance of most of the bed patients who died. The criteria on which the diagnosis of the disease is based are (1) the signs of active endocarditis, (2) fever, often of low grade, (3) positive blood cultures, most often revealing Streptococcus viridans, but sometimes another organism instead, and (4) em-

person, when affected by a respiratory infection, should resort to **bed rest** more promptly and remain in bed a longer time than the average individual. The only hope of a successful outcome lies in discovering the mild cases early and in the immediate and prolonged enforcement of bed rest. The patient in

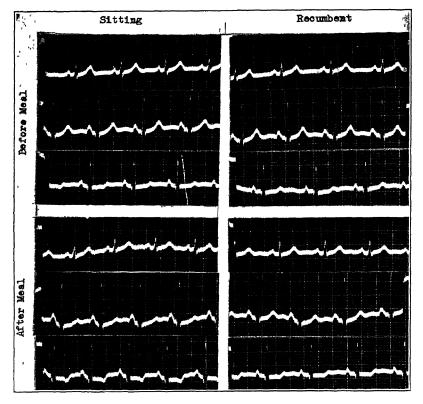


Fig 7—(Gardberg and Olsen Am Heart J)

bolic phenomena, 115, petechiae in the skin, red cells or albumin in the urine, enlargement of the spleen, or local symptoms from lodgment of bacteria in the brain, the lungs or the extremities. The commonest findings are heart murmurs and fever. Many mild cases of subacute bacterial endocarditis escape recognition because of negative blood cultures.

It is important to bear in mind that a patient with an old rheumatic heart valve or a congenital heart lesion is particularly liable to develop *Streptococcus viridans* infection. Therefore, such a

the office and dispensary who has a heart murmur and a low fever of undetermined origin may, after repeated blood cultures, show *Streptococcus viridans*, it is not in the hospital wards that mild cases will be discovered

Streptococcus Viridans Endocarditis Lenta—Further evidence in support of a close relationship between rheumatic and congenital lesions of the heart and endocarditis lenta is yielded, and the importance of the diagnostic triad—petechiae, splenomegaly, and a positive blood culture for the *Streptococcus viri*-

dans—and the grave prognosis of Streptococcus viridans endocarditis lenta is corroborated in a clinico-pathologic analysis of 88 cases of the disease at the Wisconsin General Hospital by W. S. Middleton and M. Burke.³⁹ The name Streptococcus viridans endocarditis lenta is recommended by the authors in place of subacute bacterial endocarditis in view of the current trend toward etiologic terms. Sixty of the 88 subjects were between 11 and 40 years of age, 2 cases were in the first decade, 9 in the fifth, 10 in the sixth, 4 in the seventh, and 3 in the eighth. The male sex predominated in the ratio of 5 to 3. A history of rheumatic fever alone was present in 40 9 per cent of the cases; of tonsillitis alone in 11.3 per cent, of scarlet fever alone in 15.9 per cent, and of chorea alone in 3.4 per cent. A history of congenital heart disease was found in only 4 patients Mitral murmurs predominated; and cardiac enlargement was present in 62 cases (70.4 per cent).

The *onset* was insidious in 55 cases (62.5 per cent), precipitous in 24 (27.2 per cent), and in the remaining 9 (10.2 per cent) no clinical clue to the underlying infectious process was afforded by the clinical history or the physical findings. Acute upper respiratory infections, rheumatic fever, infected abortion, dental extraction, and massage for nonspecific prostatitis apparently served as precipitating factors in certain cases

The clinical manifestations and course of Streptococcus viridans endocarditis lenta are notoriously varied and inconstant. While weakness was the commonest and the most conspicuous constitutional symptom, fever, chills, sweats, weight loss and headaches were very prominent manifestations. Contrary to the prevailing opinion, the disease occurred 5 times in patients suffering from recurrent congestive heart failure. Max-

imal temperatures of more than 102° F. (39° C.) occurred in 65 patients, and minimal levels of less than 99° F. (37.2° C.) were recorded in 77; diurnal variations of 4.1 to 8° F. occurred in 59 patients. A startling sense of euphoria accompanied some of the late remissions in the constitutional picture, and in isolated instances closely anticipated the terminal decline. Anemia of grave degree was unusual; only 5 patients had erythrocyte counts below 2 millions; levels of 2 to 3 millions were reached by 17, and of 3 to 4 millions by 34 patients. Skin petechiae occurred in 60.2 per cent of the 88 patients—the favorite sites being on the fingers or toes, in the webs of the same, and behind the ears. Petechiae were found on the mucous membranes of the mouth in 13 cases. and in the retina in 10 instances; in 3 instances the retina was the chief site of the petechial eruption.

The remarked pallor partook of a classical café au lait tint in the minority of these patients, and subcutaneous nodules were uncommon. Since the vegetations were limited mainly to the valves of the left side of the heart, emboli were encountered generally in the systemic circulation. The frequency of splenomegaly and hepatomegaly was 70.4 per cent and 43.1 per cent, respectively. In the enlargement of the liver chronic passive congestion played the important rôle. The incidence of hemiplegia was 11.3 per cent In 43 instances (48 8 per cent) red blood cells were reported in the urme. In 9 cases elevation of the basal metabolic rate, even in the afebrile periods of the disease, was observed; elevations as high at +56 per cent were recorded

As stated by Middleton and Burke, the prognosis of Streptococcus viridans endocarditis lenta is very grave. Although remissions of varying durations

and degrees are the rule, certain patients undergo a rapidly progressive decline. In this series therapy was uniformly unavailing. **Sodium cacodylate** was the drug most frequently used. **Transfusions** were given in 30 subjects; 1 patient received a total of 29 transfusions without benefit. Immuno - transfusions showed no advantage. Only 1 case of healed endocarditis lenta was found in the group.

Treatment—The numerous remedies that have been employed in the treatment of cases of subacute bacterial endocarditis in which recovery has occurred is circumstance suspicious in itself. Transfusions of blood of donors immunized with the patient's organisms have been of doubtful value. Vaccines have failed in extensive tests. In the words of Capps, "Chemotherapy has many votaries: Collargol; mercurochrome, gentian violet, arsphenamine, cacodylate of sodium, and sulfanilamide—but we cannot pin our faith to any of them Sulfanilamide has on the whole been disappointing, but it is too early to estimate its value" The patients in Capps' series who recovered, as well as most of the ones who did not, were given sodium cacodylate by vein, 3 grains (02 Gm.) a day over a period of from 6 weeks to 3 or 4 months. It is impossible to say to what extent this remedy contributed to recovery, but it probably played a minor part. The most important therapeutic measure is prolonged bed rest. Patients who recovered were kept in bed often for 3 or 4 months, and after this rest period very little exercise was allowed. The treatment was similar to that recognized as advisable in early febrile pulmonary tuberculosis

Heparin in Subacute Bacterial Endocarditis — Studies of experimental Streptococcus viridans endocarditis in dogs by M. Friedman, L. N Katz and

K. Howell⁴⁰ have indicated that the infection persisted because the constant deposition of platelets and fibrin on the vegetation exceeded the rate at which the vegetation implanted on the valve could be sterilized. Further studies on both dogs and human beings suffering from subacute Streptococcus viridans endocarditis revealed that the blood did not lack the ability to destroy the organism in vitro and that its inability to do so in vivo was due to the fact that the effective agent in the blood, the white blood cell, was unable to reach the focus of infection because of the relative avascularity of the valve leaflets and the dynamics of the blood stream flowing past the vegetations. Because of these facts it was thought possible that the prevention of new fibrin and platelet formation by the use of an anticoagulant might allow the valvular processes of repair and sterilization to gain the ascendancy and thus terminate the infection

On the basis of the above facts, a patient admitted to the Michael Reese Hospital, Chicago, with blood cultures positive for Streptococcus viridans was treated by M. Friedman, W. W. Hamburger and L N Katz⁴¹ with new concentrated heparin by continuous intravenous infusion-which has been shown by D. W. G. Murray, L. B. Jaques, T. S. Perrett and C H. Best⁴² to be effective in the prevention of thrombosis in animals and possibly in man following surgical procedures. The patient died of cerebral hemorrhage before the treatment had been continued sufficiently long to evaluate its worth. The authors felt that the danger of heparin leading to intractable or even fatal hemorrhage following the rupture of a blood vessel after embolization and the possibility of an overwhelming bacteremia following the sudden liberation of large quantities of

bacteria consequent to disintegration of the vegetations are not sufficient to discourage its use, since the disease itself is almost inevitably fatal and the possibility exists that some definite good may result.

Sulfapyridine and Heparin in Combination—Analysis of 240 cases of subacute bacterial endocarditis with positive cultures for alpha (viridans) and, rarely, gamma streptococci in Boston hospitals by S. R. Kelson and P. D. White (to be published) stressed the ineffectiveness of all varieties of therapy prior to the new chemotherapeutic drugs. Sulfanilamide, used in 24 cases, and prontosil, used in 5, temporarily improved a few; sulfapyridine, used in 4 cases, although not curative, appeared far more effective. Data collected from other clinics and from 1 case report concerning 66 cases in which intensive treatment was given with sulfapyridine confirm the impression that in most instances the drug lowers the temperature and sterilizes the blood stream, but that these effects pass off in from a few days to a month or, rarely, more.

In subacute bacterial endocarditis the streptococci lie as a rule near the periphery of the vegetations, a mass chiefly of fibrin, an ideal culture medium and protective barrier, and of platelets, polymorphonuclear leukocytes are scarce or absent in the vegetation, and at its base, fibrosis is a nearly constant finding At present it appears impossible to increase the number of phagocytes and draw them into contact with the bacteria, to dissolve the vegetations or to induce granulation within them. However, an attempt might be made to prevent thrombotic deposition on their surface in order to (1) restrict the nidus and culture medium for bacterial growth, (2) prevent embolism from the freeing of fresh thrombus, and (3) check the growth of the vegetations so that proliferating fibroblasts may fill in the areas thus limited. On the basis of these considerations, S. R. Kelson and P. D. White⁴³ have treated 6 patients with subacute and 1 patient with acute Streptococcus viridans endocarditis with sulfapyridine and an anticoagulant, crystalline heparin.

Details of the method of treatment are as follows: "The contents of a 10 cc. vial of heparin (10,000 units) are added to 500 cc. of physiologic solution of sodium chloride, and such a solution is given by uninterrupted intravenous drip day and night for 14 days. The rate of flow (usually from 15 to 25 drops a minute) is carefully regulated to maintain, as well as possible, the venous clotting time (normally below 20 minutes) at approximately 1 hour. Clotting time is measured before treatment, twice or more the first day and then at least daily by the 5-tube method of Lee and White. Heparin is begun from 4 to 7 days after sulfapyridine has been started, when nausea and vomiting have subsided and before 'escape' from its effects has occurred From 60 to 90 grains (4 to 6 Gm.) of sulfapyridine (with desired blood levels of 5 mg per hundred cubic centimeters or more) are given daily by mouth before and during the use of heparin and for 1 week afterward—a total of about 4 weeks. Blood transfusions are given if there is anemia of 3,500,000 red blood cells or below. Persisting infections (including this one) predispose to vitamin C deficiency, which interferes with fibrous repair, all patients, therefore, are saturated with 200 mg. of ascorbic acid by mouth 4 times a day for 3 days and continued on 100 mg. a day. Other added vitamins and iron are not essential to the therapy."

Two of the patients, 1 with subacute and 1 with acute endocarditis, were able

to take the heparin for only an hour and a half because of reactions to a toxic lot of the drug, too short a time to expect any lasting effect on the thrombus formation. Two other patients were able to continue the heparin for only 3 days and 2 days, respectively, because of the serious course of the disease itself which terminated fatally in a short time (2 weeks or less). The remaining 3 patients who were able to take the heparin for more than a week, a length of time probably adequate to produce an important effect on thrombus formation, showed striking improvement and have been free from evidences of the disease for 19 weeks, 18 weeks and 4 weeks, respectively, after discontinuing treatment

The possible danger of excessive bleeding incident to embolism in these cases is recognized by the authors, but it is believed fair to accept this risk in the face of the hopeless prognosis of the disease. The treatment is still in the experimental stage, and is not to be advised except under close and careful observation and preferably in the earlier cases or less seriously ill, and there must be no doubt about the diagnosis.

Standardization of Blood Pressure Determinations

It has long been realized that wide variations in the blood pressure records of the same individual are due not only to changes in the pressure from time to time in different conditions but also to difference in the methods and interpretation used by the observers. And recently this opinion was confirmed by a survey made by I. S. Wright, R. F. Schneider and H. Ungerleider. As a consequence, committees of the American Heart Association and of the Cardiac Society of Great Britain and Ireland have recommended the follow-

ing procedure as the standard method for taking and recording blood pressure readings in man:

- 1 Blood Pressure Equipment The blood pressure equipment to be used, whether mercurial or aneroid, should be in good condition and calibrated at yearly intervals—more often if defects are suspected. (Mercurial preferred—British Committee.)
- 2 The Patient The patient should be comfortably seated (or lying—British Committee), with the arms slightly flexed and the whole forearm supported at heart level on a smooth surface. If readings are taken in any other position, a notation of that fact should be made. The patient should be allowed time to recover from any recent exercise or excitement. There should be no constriction of the arm by clothes, etc.
- 3 Position and Method of Application of the Cuff—A standard-sized cuff containing a rubber bag 12 to 13 cm in width should be used. A completely deflated cuff should be applied snugly and evenly around the arm with the lower edge about 1 inch above the antecubital space and with the rubber bag applied over the inner aspect of the arm. The cuff should be of such a type and applied in such a manner that inflation causes neither bulging nor displacement.
- 4 Significance of Palpatory and Auscultatory Levels In all cases palpation should be used as a check on auscultatory readings. The pressure in the cuff should be quickly increased in steps of 10 mm. Hg until the radial pulse disappears, and then allowed to fall rapidly. If the radial pulse returns at a higher level than that at which the first sound is heard, the palpatory reading should be accepted as the systolic pressure, otherwise the auscultatory reading should be accepted.
- 5 Position and Method of Application of Stethoscope The stethoscope should be placed over the previously palpated brachial artery in the antecubital space, not in contact with the cuff. No opening should exist between the lip of the stethoscope and the skin, this should be accomplished with the minimum pressure possible. The hand may be pronated or supinated, depending on which position yields the clearest brachial pulse sounds.
- 6 Determination of the Systolic Pressure—The cuff should be rapidly inflated to a pressure about 30 mm above the level at

which the radial pulse can be palpated. The cuff should then be deflated at a rate of 2 to 3 mm. Hg per second. The level at which the first sound regularly appears should be considered the systolic pressure, unless, as pointed out above, the palpatory level is higher, in which event the palpatory level should be accepted. This should be noted.

7. Determination of the Diastolic Pressure and the Pulse Pressure-With continued deflation of the cuff, the point at which the sounds suddenly become dull and muffled should be known as the diastolic pressure. If there is a difference between that point and the level at which the sounds completely disappear, the American Committee recommends that the latter reading should be regarded also as the diastolic pressure. This should then be recorded in the following form. RT* (or LT†) 140/80-70, or 140/70-0 levels are identical the blood pressure should he recorded as follows: 140/70-70. The cuff should be completely deflated before any turther determinations are made.

The British Committee believes that except in aortic regurgitation it is nearly always possible to decide the point at which the change comes, and that this is the only reading which should be recorded

General Considerations—In the case of the mercury manometer the level of the mercury at rest should be exactly at the zero mark, the apparatus must be on a level surface, and the small air vent at the top of the glass tubing must not be allowed to become clogged. In the case of the aneroid type of instrument a yearly calibration against a U-tube standard is recommended, when the apparatus is completely deflated the needle should stand at zero, and should move immediately when the inflation begins

Inquiry should be made as to the patient's activity just before the examination, and a rest period of from 10 to 15 minutes prior to making the blood pressure readings should be allowed to eliminate or minimize any disturbing physical and psychologic factors which

might be present. As there are variations in the blood pressure level of certain individuals in the course of a day. the observations should be made at essentially the same time and in the same relationship to meals, sleep, exercise and other similar factors. On the first examination the blood pressure should be taken in both arms since the 2 may not be the same. And in the presence of unexplained high pressure in the brachial artery, it is suggested that blood pressure in the legs be taken also, as by this procedure conditions such as coarctation of the aorta may be detected. Unnecessarv venous congestion should be avoided by making certain that there are no constriction bands on the arm and that the pressure cuff is not inflated longer than necessary to make the blood pressure reading. For blood pressure readings of the thighs, the auscultation should be over the popliteal artery with the patient prone.

When premature beats are present the higher systolic pressure of the beats that terminate compensatory pauses should be ignored. With auricular fibrillation both diastolic and systolic readings should be recorded as approximate only. the average of a series of readings for the reappearance of sound should be noted as the systolic pressure and similar averages for the fourth and fifth "points" should be recorded as the diastolic pressure. Alternation of the pulse during blood pressure determinations may indicate left ventricular weakness In occasional instances the usual sounds are heard over the brachial artery at a high level, and as the pressure is reduced, the sounds disappear only to reappear at a distinctly lower level. This zone of silence is known as an auscultatory gap, and its existence is important as it is possible in such cases to inflate the cuff only to the level of the auscul-

^{*} RT = right arm

[†] LT = left arm

tatory gap and to record the systolic pressure at the level where sounds are first heard, which may actually be 40 or 50 mm. below the true systolic level. When especially careful studies of the blood pressure are to be made, the use of basal blood pressure conditions, with

foot cradle consists of: (1) A 60-watt electric light bulb (A, Fig. 8); (2) an electric light socket and switch, cord, and plug for connection with house current; (3) a simple adjustable thermostat with thermometer (B, Fig. 8); (4) a piece of $\frac{1}{32}$ inch hard black vulcanized

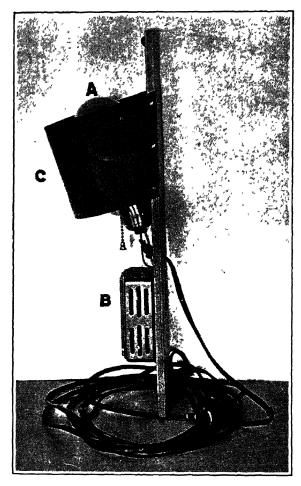


Fig 8—A simple thermoregulator for maintaining optimum temperature in a foot cradle A, 60-watt bulb, B, thermostat, C, lamp guard (Montgomery and Starr Am J. M Sc)

preparation similar to that used in making a basal metabolism test, should be considered.

Peripheral Vascular Disease

Physiotherapeutic Devices in Treatment—H. Montgomery and I Starr⁴⁶ describe 4 types of apparatus. A simplified form of thermoregulator for maintaining optimum temperature in a

fiber sheet, 12 inches by 16 inches; (5) a piece of copper sheeting, $\frac{1}{32}$ inch thick, 1 inch by 6 inches, and (6) a board for mounting approximately 17 inches by $3\frac{1}{2}$ inches by $\frac{1}{4}$ inch. The total cost of the materials is approximately \$10, while the cheapest apparatus on the market sells for \$50. The apparatus is mounted on the board, the copper sheet being bent to support the light socket. Two layers

of the fiber sheet are bent around the light bulb; the inner layer must be at least ½ inch from the bulb at the nearest point. The outer layer is fastened upon the inner layer at the mounting board, but extends 1 inch beyond the inner layer at the greatest distance from the mounting board. In assembling the apparatus, there must be absolute certainty that the patient's foot cannot come into contact with either the bulb or the inner layer of

diameter, ½6 inch wall, with flamed ends—to fit the fingers loosely (Fig. 9); (2) surgical drainage tubing 1 or 1½ inches across when lying flat; (3) one No. 6 rubber stopper with hole bored to fit a (4) glass or metal connecting-tube running to (5) a rubber bulb with single opening and without valves ("blind bulb"), 1½ inches by 2½ inches, which must give negative pressure of 100 mm. Hg. The drainage tube is employed as

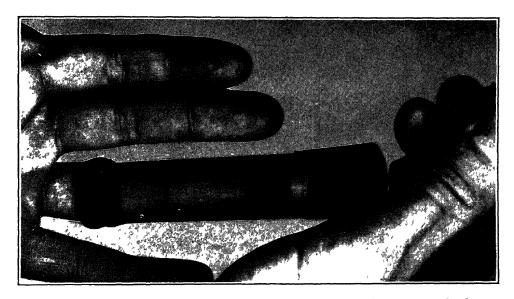


Fig 9—A simple apparatus for application of alternate suction and pressure to the fingers (Montgomery and Starr Am J M Sc)

the guard. The apparatus is hung inside any leg cradle with the lamp end up The thermostat is adjusted, usually by the patient himself, until a maximum of comfort is obtained, the temperature selected usually is between 85 and 95° F. (29 5 and 35° C).

A simple apparatus for the application of alternate suction and pressure to the fingers of cases in which the digital arteries are mainly involved and the outstanding complaint is of an indolent lesion localized to a digit has been made at a cost less than \$1. Its construction calls for (1) a section of glass tubing—a piece 5 inches long of 1 inch internal

a cuff to make an airtight joint between finger and glass tube; and lanolin is used to make the joint between cuff and finger airtight Tight constriction of the finger by the rubber is to be avoided, and it is unnecessary The bulb is attached when it is partly compressed. Suction is applied to the finger by allowing the bulb to expand, and pressure is applied by compressing the bulb with the fingers of the other hand Four patients with advanced thromboangutis obliterans of the fingers have been treated, the patients taking the apparatus home with them for continued treatment Treatment consisted of suction for 10 seconds, then

of pressure for a sufficient length of time to make the fingers blanch—which procedure was followed a half hour twice daily. In each instance, after 2 weeks to 3 months of treatment, a cold, blue, painful finger became warmer, its color improved, and pain disappeared.

Iontophoresis — An apparatus for giving drugs by iontophoresis has been

can easily be made—makes excellent contact, has long life, and has given rise to no more than a mild erythema when 10 to 35 milliamperes of current have been used. The positive electrode consists of a 15 inch by 2½ inch piece of diathermy metal sheeting, "medium electrode foil," obtainable from any roentgen ray supply store, reinforced absestos paper

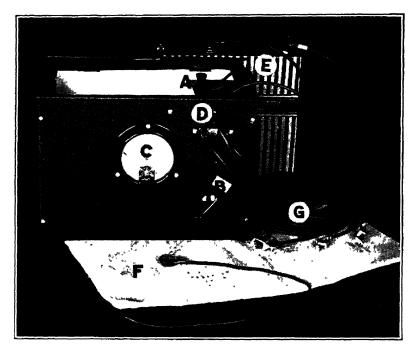


Fig. 10—Apparatus for iontophoresis. A, Portable battery; B, variable resistance. C, milhammeter, D, tip jacks, E, long-life battery, F, negative electrode, G, lead wires. H, alligator clips. I, terminal of negative electrode. (Montgomery and Stari. Am. J. M. Sc.)

constructed from standard radio parts for about \$15 (Full details regarding the assembling of the apparatus are presented in the original article — En) The negative (indifferent) electrode (F, Fig 10 or 10A), for application to the back of the thorax, consists of copper wire screening with edges heavily covered with sewed cotton tape, covered by oversize (to allow for shrinking) light duck. An end of rubber-insulated wire is braided and tied by cotton thread into one end of the copper screening. This electrode—which cannot be bought, but

(Merck and Company), and a 3-mch Ace bandage

In the use of iontophoresis, the negative electrode is prepared by soaking it and a hand towel in warm tap water, the electrode is then placed on a small mat of rubber laid on turkish toweling which covers the couch (first covered by a rubber sheet), and the wet hand towel is placed on the electrode. The patient, wearing only a hospital gown with an open back, reclines on the couch with the wet towel in contact with his back. Either 1 or 2 positive electrodes may be

used. The asbestos paper and the Ace bandage are soaked in a 0.2 per cent solution of mecholyl (acetyl-beta-methyl-choline chloride); and the part to be treated is surrounded by 1 layer of wet asbestos paper. Two more layers, each a little larger than the metal sheeting, are laid on the first layer, and the metal sheet is laid on this triple thickness of paper. The bandage is firmly applied

paper and gets into direct contact with the skin. The patient must be instructed to report any discomfort immediately.

Iontophoresis usually is given 3 times weekly for periods of ½ hour each time. Of 8 patients with varicose ulcers treated by mecholyl iontophoresis, 1 was unimproved, 3 were healed, and 4 much improved after treatment for periods varying from 1 week to 4 months; of 8

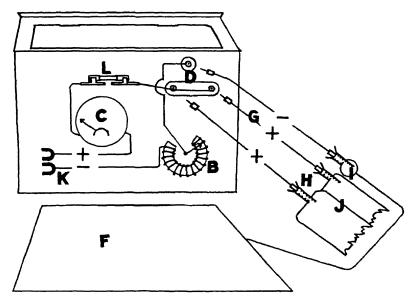


Fig. 10.4—Apparatus for iontophoresis—Wiring Diagram. Designations by letter correspond to those in Fig. 3. J, Metal sheeting of positive electrodes, K, spade lugs, L, fuse (Montgomery and Starr: Am. J. M. Sc.)

around all of the asbestos paper and all except one end of the metal sheet (I, Fig 10A); this end is left free and the black lead wire is clipped to it. Several minutes should be used in raising the current to the desired level A strong prickling sensation in the positive or negative electrode indicates that tolerance has been reached, but this sensation becomes less and then more current can be tried. There should be no discomfort during treatment, and from 15 to 25 milliamperes can be used with safety in most cases The chief danger lies in the burn which will result if the metal of the positive electrode slips off the underlying

patients with chronic thrombophlebitis, similarly treated, 7 were symptomatically relieved in from 1 week to 4 months; and of 4 patients with scleroderma, 3 were definitely benefited in from 2 weeks to 8 months. Only a few untoward effects were encountered. In an asthmatic patient with a varicose ulcer, mecholyl iontophoresis (8 milliamperes of current) produced an asthmatic attack; and in 1 patient with severe chronic thrombophlebitis and varicose veins, 2 treatments were followed by chills and fever. In the latter case it is reasonable to suppose that bacteria or toxic materials were washed from diseased vessels

into the general blood stream, since it has been demonstrated that the blood flow through a limb is greatly increased by mecholyl iontophoresis.⁴⁷

In view of the fact that some patients with peripheral vascular disease find relief from pain on hanging their diseased legs over the side of the bed, an old hospital bed has been altered to permit a

to alter the bed was about \$50. When in use a blanket is placed over the box, so that one edge acts as a curtain to close the aperture through which the feet are inserted; the bedclothing is then thrown over the top of this blanket. Most patients have preferred to have their feet about 30 degrees below horizontal when the back rest is down, and

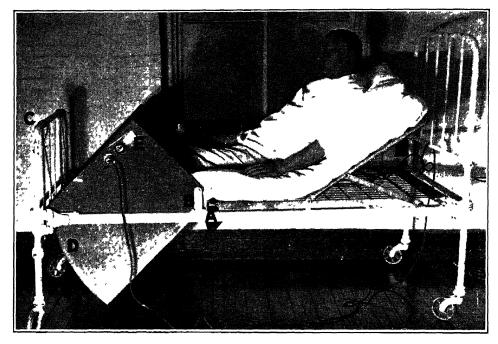


Fig 11—A bed altered to permit a dependent position of the legs (Montgomery and Starr Am J M Sc)

comfortable dependent position of the legs, by shortening the spring as shown in Figure 11 to a point (A) 30 inches from the foot of the bed Inside the spring frame a box is mounted on a hinged pedestal (B) so that it can be raised and lowered by cords (C) tied to the foot to support the free end at the desired height The box contains 2 lights, shielded with Masonite guards, placed 1 on each side, under the letter D, which are controlled by a DeKhotinsky Thermoregulator, the outer end of which is shown at the apex of the box (E). The total cost of the materials and labor

45 degrees or more when the back rest is elevated. The relief afforded is often quite striking. It must be borne in mind, however, that certain patients with peripheral vascular disease complicated by infected lesions or by edema, have increased pain when the diseased leg is dependent, and that such patients are never treated with the legs in the dependent position.

Treatment of Deep Thrombophlebitis and Chronic Leg Ulcers with Acetyl-beta-methylcholine Chloride Iontophoresis—Until recently the treatment of postphlebitis edema has been far from satisfactory. Elastic supports, massage, heat, and light are therapeutic gestures and nothing more in many instances; extract of leeches has been advocated, but as yet little is known of its value; and the Kondoleon operation is a formidable procedure. Good results with acetyl-beta-methylcholine chloride iontophoresis have been obtained by R. A. Sokolov and M. P. Meyers⁴⁸ in 18 of 19 patients with deep thrombophlebitis and in 13 cases of chronic leg ulcers of various etiology. In 12 of the latter cases the ulcers were completely healed. and in the 13th the lesion was healing rapidly when last observed. The technic of the treatment was essentially the same as that used by J. Kovacs,49 with the exception that 0.1 per cent was found to be as effective as the higher concentrations previously recommended. The individual treatments were as a rule of 45 minutes' duration; the first 6 to 10 treatments were given at daily intervals; and subsequently—as improvement permitted-treatments were reduced to 2 or 3 weekly.

The shortest duration of the deep thrombophlebitis among the patients treated was 8 days, the longest 32 years. In the cases of old chronic phlebitis it was not unusual to see no alteration in the disease process until considerable time had elapsed, and then suddenly to observe changes taking place. marked improvement was observed in instances in which the disease was not of too long standing Criteria of improvement were (1) diminution in the size of the limb as determined by measurements taken circumferentially at the level of the largest diameter of the calf and at the level of the malleoli; (2) improvement in ability to walk and stand; (3) ability to resume previously impossible occupations or tasks; (4) freedom or relief of subjective symptoms such as pain, heaviness of the legs, or "stiffness" of the legs. In the ulcer cases clinical improvement was manifested shortly after treatment was started. After 2 or 3 applications a healthy red granulation tissue appeared at the base of the ulcer; and soon growth of epithelium became evident at the border, and by the end of 6 or 7 days measurable differences in the size of the lesions were apparent.

Treatment of Occlusive Arterial Disease of the Legs by Means of Sanders Vasocillator (Sanders Bed) —The value of a motorized oscillating bed⁵⁰ has been investigated by N. W. Barker and G. M. Roth⁵¹ in a study of 88 cases of occlusive arterial disease of the legs at the Mayo Clinic. The 88 cases consisted of 38 cases of arteriosclerosis obliterans without diabetes mellitus, 16 cases of arteriosclerosis obliterans with diabetes mellitus, 31 cases of thromboangiitis obliterans, 2 cases of embolic arterial occlusion, and 1 case of traumatic arterial occlusion. No contraindications to the use of this method of treatment were found, with the possible exception of the presence of marked infection in association with gangrene.

The Sanders bed-which recently has been accepted by the Council on Physical Therapy of the American Medical Association under the name "Sanders vasocillator"52—consists of an ordinary hospital bed attached to a special cradle, so that the bed can be rocked on a transverse axis across its midportion By means of an electrical motor the bed is tipped on its transverse axis continuously, so that the head of the bed is alternately raised and lowered through an arc of approximately 60 degrees. The period of oscillation can be adjusted to take from 1 to 7 minutes for a complete cycle. It is possible to change the midposition of the bed through a small arc, so that, in the extreme positions, the head of the bed

may be higher and the foot lower at the end of the cycle, or vice versa. The head and foot of the bed are hinged so that either can be raised, and the patient made to lie in the semirecumbent position with the thighs and knees partially flexed.

In using the bed it is important to have the patient in a comfortable position, and to secure enough flexion of the thighs and knees so that when the head a definite soporific effect. Since ordinary sleep causes vasodilatation, sleep may have been partly responsible for the rise in skin temperature observed.

The bed can be used for comparatively short periods, or patients can be kept on it continuously for days or weeks. In comparison with other mechanical methods of treatment of peripheral circulatory diseases, it possesses the advantage of avoiding any constriction of the

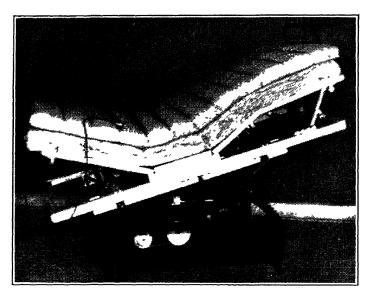


Fig. 12—For peripheral vascular diseases. The telescopic pitman is adjusted with crank and set so that the cycle of low foot and high foot will be equal. (Sanders: $J \land M \land A$)

of the bed is at its maximal elevation the patient's body does not slip toward the foot of the bed Also adjustments of the bed are usually necessary for each patient, and usually it is advisable to run the bed at a rather rapid speed (cycle of 2 minutes) It is desirable to have the feet of the patient just become blanched when they are in the elevated position and just develop rubor when in the dependent position before the direction of motion changes One interesting effect of the bed is that the majority of the patients become rather sleepy after being on it for a comparatively short time, the oscillating movement apparently having

legs or obstruction to the venous circulation It can be used in conjunction with vasodilating procedures, such as artificially induced fever, drugs given by mouth, or increased environmental heat Treatment produces slight objective improvement of circulation and slight, but incomplete, vasodilatation. Its most striking therapeutic effect appears to be the immediate relief of pretrophic pain, the pain of ischemic neuritis, and the pain of ulceration and gangrene Relief of these types of pain is not necessarily maintained when the treatment is discontinued The bed apparently has minimal, if any, beneficial effects on the pain

of intermittent claudication. The authors feel that it constitutes a valuable addition to the armamentarium for the treatment of peripheral arterial diseases, but it should not supplant other methods of treatment.

Deproteinated Pancreatic Extract (Depropanex) in the Treatment of Intermittent Claudication Due to Arteriosclerosis Obliterans — The effect of deproteinated pancreatic extract ("depropanex" -- prepared by Sharp and Dohme Laboratories) in the treatment of intermittent claudication has been studied by M. M. Fisher, A. W. Duryee and I. S. Wright⁵³ in 27 patients with definite arteriosclerotic disease of the extremities, with aid of an ergometer, consisting of a vertical stand fitted with a foot pedal which, when depressed, raised a weight of 136 pounds. There were 24 males and 3 females, all of whom were ambulatory, varying in age from 50 to 80 vears, the average age being 62 years. None had gangrenous lesions. Thirteen had received no previous treatment for their vascular disease: 14 had received treatment, such as other tissue extracts, suction-pressure, or intermittent venous occlusion-which was discontinued before the tests with the pancreatic extract were begun. All of the patients were advised not to use tobacco, and were instructed to take warm foot baths nightly, wear warm socks and shoes, and take proper care of the nails and corns Each patient was carefully studied by means of oscillometric readings, roentgenograms, arteriograms, and other procedures.

After resting by sitting for one-half hour a control test was made. During the test the patient stood upright on the ergometer in the same position as held in walking, with the foot of the extremity to be tested on the pedal, and was paced at 120 steps per minute with a stop-

watch or metronome. He was not allowed to stop until the pain, cramp, or fatigue in the calf or thigh became so severe that he was unable to continue. Then after another rest of 1 hour's duration, a second control test was made. In most instances, the times for these 2 tests were very nearly identical. Three cubic centimeters of deproteinated pancreatic extract were injected intramuscularly after the second test: one-half hour later a third test was made. After the original tests the treatment consisted of 3 cc. of the deproteinated pancreatic extract intramuscularly triweekly. The tests were rechecked frequently. Patients have been followed as long as 9 months.

Of 8 patients with untreated, uncomplicated, arteriosclerotic vascular disease, 6 showed improvement and 2, no improvement, with the initial tests; but all of those receiving 10 or more treatments were benefited. Of 5 patients, untreated, but with complicating diabetes, heart disease, varicose veins, or other abnormalities which might have had a relationship to this condition, 4 showed improvement and 1, no improvement, with the initial tests, but 4 were improved after 10 or more treatments, and the 1 patient who was not benefited by the initial test was not treated. And of 14 patients—some with and some without complicating diseases—who had been treated previously, 13 showed improvement after the initial test, and in 1 instance benefit was so slight as to be inconsequential, but all of 10 who received 10 or more treatments showed improvement Before treatment the average number of New York City blocks which had to be walked to produce intermittent claudication was for the entire group about 2, while after 10 or more treatments the average was about 8, an increase of 400 per cent-which com-

pared favorably with the 300 per cent improvement as measured by the apparatus. Injection of physiologic saline solution failed to produce an increase in claudication time under identical conditions.

The mechanism of the action of pancreatic tissue extracts has never been satisfactorily explained, although a hormonal or replacement action similar to that of insulin is the most popular theory. Assay studies on animals, in which its antagonistic action to adrenalin has been demonstrated, indicate a vasodilatation factor. The most satisfactory dose of the deproteinated pancreatic extract appears to be 3 cc., given intramuscularly on alternate days, larger doses did not seem to produce more beneficial results nor a more prolonged action. No untoward reactions were observed in more than 1000 injections. It has been given intravenously to 20 patients without severe systemic reactions; but this method of administration is not advocated at this time.

Of 100 patients followed for a period of 4 to 6 months while under treatment with deproteinated pancreatic extract, 74 reported definite clinical improvement. But attention must be given to the fact that spontaneous improvement and regression are common in intermittent claudication due to peripheral arteriosclerosis, and that only by studying a group of patients over a long period of time with a standard method of testing may conclusions be drawn as to the value of any therapeutic measure

Papaverine Hydrochloride in Treatment of Peripheral Vascular Disease—The effectiveness of papaverine hydrochloride intravenously as a vasodilator has been studied by D. Littauer and I. S. Wright⁵⁴ in a series of 18 subjects, which included 13 with thromboangitis obliterans, 3 with arte-

riosclerotic obliterans and 2 normals. Compared with the degree of vasodilatation obtained by immersion of the opposite pair of extremities in warm water at a temperature of 107.5 to 115° F. (42 to 46° C.), papaverine hydrochloride was found to be ineffective and uncertain in action. Following water immersion, vasodilatation was obtained in 11 (61 per cent) of the 18 subjects examined, while following papaverine hydrochloride injected into an anticubital vein in the amount of $\frac{1}{2}$ grain (0.03 Gm.) and repeated between 30 and 45 minutes later, only 3 (17 per cent) exhibited any appreciable degree of vasodilatation as measured by changes in skin temperature and in appearance of the skin. On the other hand, I patient, who did not show relaxation of vasomotor tone following water immersion, did respond to injections of papaverine hydrochloride.

Following water immersion, 2 of 4 patients with Raynaud's syndrome showed a rise of temperature of the fingers and change of appearance of the fingers from dead white or purplish cyanosis to healthy pink, in 1 no response was obtained, and in the fourth it was impossible to secure constant readings as the vasospasm came and went frequently. In all 4 cases papaverine had no vasodilating effect at the temperatures at which spasm could be maintained.

In a group of 4 cases of acute peripheral embolism and 2 cases of thrombosis within a few hours after the accident, 5 of whom were given large doses of papaverine by mouth and intravenously, and the sixth "spasinalgin" (a proprietary preparation containing papaverine), and all of whom were also treated variously with sedatives, warmth, alternating suction and pressure, and the oscillating bed, the clinical results were what might have been expected if papaverine had not been added to the thera-

peutic regimen. One patient (45 years of age) experienced a return of circulation, and the remaining 5 (all but 1 of whom were over 50 years of age) developed dry gangrene, necessitating amputation, or died. It is the opinion of the authors that spontaneous recovery, which frequently occurs without any therapy in acute embolism or thrombosis of the vessels of the extremities, might explain the seeming benefit following the use of papaverine reported by various investigators.

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DERMATOLOGY

By John B. Ludy, M.D.

PYOGENIC INFECTIONS OF THE SKIN

Impetigo Contagiosa

Impetigo contagiosa is produced by uncomplicated superficial infection of the skin by the streptococcus. This organism can be obtained in pure culture from the clear bullous fluid of eruptions appearing in early stages This fluid becomes contaminated with staphylococci in later stages. The fluid contents of bullae coagulate to form crusts which can usually be discerned as white, sodden, epidermal tags at the periphery of lesions. Individual lesions are usually selflimited The duration of eruptions is dependent upon autoinfection and the development of fresh bullae. Individual lesions may occasionally persist to form considerable epidermal involvement which may extend into the dermis and lead to considerable destruction and This involvement may occur necrosis on the scalp, below the nose, on the lower lip, and on the legs (ecthyma) sites of predilection are the face and scalp Very rarely, impetigo becomes generalized

Complications — Fissuring develops at the deepest portion of areas of impetigo when the disease attacks folded regions. The inflammatory reaction may change its character in these areas, gradually assuming the nature of an eczematous dermatitis. The course of eruptions is altered in these circumstances from that of isolated self-limited lesions to lesions which tend to persist for indefinite periods. No explanation can be offered to explain this transformation beyond the anatomical situation of primary lesions. Such phenomena are

commonly met with in the regions of the retroauricular folds and at the corners of the mouth. The resulting dermatitis is identical with that developing spontaneously in the retroauricular region known as "seborrheic dermatitis" This homology favors the opinion that the term "seborrheic dermatitis" should be discarded and that all forms of dermatitis in the retroauricular region be considered infectious in origin and that the streptococcus is the infecting agent is practically impossible to differentiate between the spontaneously arising dermatitis and the postimpetiginous variety The scalp may become involved by dermatitis extending from the retroauricular region Another frequent location is to the anterior cubital fossae dermatitis may also occur spontaneously in the natal fold, and the folds in the groins and inframammary regions Multiple flexural involvement is typical of the fully developed syndrome known as "seborrheic dermatitis" Considerable justification is therefore in favor of regarding the syndrome as a manifestation of streptococcal infection rather than as 1 due to "seborrhea" because the seborrheic state, in the majority of cases. is conspicuously absent. The treatments of flexural "seborrheic" dermatitis and impetigo are essentially the same except for the fact that each stage in treatment is extended over a more prolonged period.

It is not uncommon to observe in severe and extensive impetigo the development of a generalized secondary erythema. This erythema is obviously of internal origin, and probably the result of streptococcal toxemia.

Diagnosis—Impetigo is characterized by the appearance of isolated vesicles or bullae. The discrete and isolated nature of vesicles differentiates it from the lesions of dermatitis. The localized distribution of vesicles or bullae and their obvious infectivity differentiate them from the vesicular or bullous eruptions of internal origin, such as dermatitis herpetiformis, pemphigus, bullous urticaria. and the vesiculo-bullous exanthemas. It is only in rare cases of generalized bullous impetigo that the diagnosis becomes confused. The transient nature of bullae in impetigo, their distribution and the tendency to early crusting should simplify differential diagnosis in these rare cases.

Impetigo may complicate an already existing skin lesion with the result that the nature of both diseases becomes altered. The bullae of impetigo in this case may not be much in evidence because of the pre-existing skin disease. The exudation and crusting in the original lesion are also greatly exaggerated. This secondary impetiginization is likely to occur in lesions which are in themselves exudative, lesions involving folded regions, and in scabies in which scratching The advent of an impetigo is violent interferes with the treatment of the original disease which treatment is interrupted until the complication is corrected.

Treatment—The treatment of impetigo resolves into allaying the inflammatory process in lesions; destroying the infecting organism, and controlling scratching, and obviating infected material from contact with the skin, thus preventing new lesions in forming. This is best attained in the early exudative stage by employing a 2 per cent aqueous solution of gentian violet in conjunction with boracic-starch poultices. Gentian violet is painted over affected areas once a day. Starch poultices are applied 3 times

a day. Failure of impetigo to respond to starch poultices is almost always the result of badly made jelly for this purpose. Starch poultices absorb the exudate and prevent crust formation. Applications of starch-jelly should be from ½ to ¾ of an inch thick. Existing crust formations soften with poultice application and this renders removal easy. Washing affected areas twice daily removes softened crusts. The exudative phase subsides after a few days of treatment by this method. A 1 per cent ammoniated mercury paste is applied twice each day after subsidence of exudation. Soap and water are used to cleanse the parts once each day. It is advisable to apply the paste spread on muslin cut in forms of masks or in suitable strips kept in position with bandage Spread of lesions of impetigo through scratching is minimized by keeping involved areas constantly covered with dressings

Impetiginous lesions of the chin and the nostrils are difficult to treat in children because these areas are frequently moist at this age. Dabbing the area several times each day with 1 per cent aqueous solution of silver nitrate is useful. The application of elastoplast is often helpful

The hair surrounding impetiginous areas of the scalp is clipped. Involved areas of the scalp are painted with gentian violet or ammoniated mercury paste. It is practically impossible to apply starch poultices on the scalp unless the entire scalp or a large area of the head is shaved

Cellulitis rarely complicates impetigo even when the palms and soles are involved Bullae on the palms and soles tend to persist for long periods unless lesions are snipped by removing the thick horny layer of the skin which forms on these lesions

Attention is given to the general health of the patient with recurring impetigo. The skin, clothes, and bedding are kept scrupulously clean. Vaccines are not beneficial in treating impetigo. The sulfanilamides have not as yet been useful for treating this disease.

Streptococcal Paronychia

Chronic inflammatory paronychia of 1 or more nail folds may occur from streptococcal infection. The condition may be associated with impetigo elsewhere in the body, a combination frequently occurring in children It is met with frequently among adult females who are engaged as washerwomen, or who carelessly manicure their nails. It also occurs in both sexes in association with any long-standing dermatitis of the hands and fingers The nail fold becomes red and tender The cuticle disappears or remains as a ragged vestige. The nail fold retracts from the nail plate and leaves a deep cavity from which pus may sooner or later exude Streptococcal paronychia of children usually disappears spontaneously and yields more readily to treatment Streptococcal paronychia of adults persists for an indefinite period if untreated and slowly responds to treatment The condition cannot be regarded as cured until the cuticle has been restored completely. Considerable temporary deformity of the nail plate may result from prolonged inflammation of the nail base

Treatment—Streptococcal paronychia does not respond readily to treatment. It may be necessary in the early stages of the malady to employ *boracic soaks* for a few days to reduce the discomfort, edema, and purulent discharge. The patient should avoid working in wet occupations.

Local daily treatment consists of applying 2 per cent aqueous solution of carbol fuchsin. Liquid carbolic acid

is also applied once a week. Both liquids are painted on the nail plate, nail fold, and particularly within the cavity between them. A streptococcal vaccine is helpful in paronychia. This is given in an initial dose of 5 million, increasing the dose to 50 million at weekly intervals over a period of 6 weeks. A concentrated preparation of vitamin D can be given over the period of a few weeks. Irradiation by a small dose of roentgenrays is helpful after granulations have formed within the cavity at the base of the nail.

Staphylococcal Infections

The characteristic reaction of the skin to staphylococcic infection is cellular in type when contrasted with that of streptococci. The lesions resulting from staphylococcic infection are a pustule, a furuncle, or a cutaneous abscess. The variance from pustule to cutaneous abscess depends upon the depth of infection. The organisms may enter the tissue following gross injury to the skin The lesions are, however, localized to the pilosebaceous glands. The sweat glands and their ducts are less frequently in-The Staphylococcus albus or aureus are always present on the human skin It is impossible to explain why the organism changes its parasitic existence to a pathogenic course. Primary pustulation occurs on areas covered with hair. The presence of hair in the hair follicles seems to be necessary for infection

Recurring pustulations almost invariably involve areas covered with hair, such as the bearded region (sycosis), scalp, pubes, groins, and legs. The condition is more commonly met with among males. Recurring furuncles may affect a localized area Particular attention is called to the buttocks, forearms, and the back of the neck as sites of predilection.

A widespread staphylococcal folliculitis may develop suddenly for no apparent reason. A single pustule may appear and an extensive rash may slowly spread from it. An injury occasionally marks the onset of eruption. An outbreak may also occasionally follow the application of oily hydrocarbon preparations to the skin and from the internal administration of iodide or bromides.

Treatment—It is best to let folliculitis run a short, undisturbed course to permit its mumification. The lesions should be protected by *elastoplast* to prevent friction and contamination of adjacent hair follicles.

A prolonged course of treatment is necessary when a chronic folliculitis is complicated by dermatitis The affected area is shaved and kept denuded of hair. Muslin soaked in olive oil may be applied for a few hours before shaving to remove crust formation and facilitate the shaving All forms of greasy applications are avoided Boracic starch poultices or wet dressings of a 05 per cent watery solution of silver nitrate are employed. A 2 per cent solution of gentian violet in water is painted on once each day for 2 consecutive days after the intensity of the inflammation and crusting has reduced Starch poultices are again used the following day Gentian violet may be incorporated in poultices by painting before they are applied on involved areas. The next step is to apply crude coal tar. It is a curious fact that pustulation is greatly aggravated whenever tar is applied in ointment form on lesions of folliculitis whereas it can almost always be used with benefit in its crude form as a paint. Crude tar is painted thinly. A dusting powder is applied a few minutes later to make drying complete in about 15 minutes From 36 to 48 hours after application the tar is cleaned off with olive oil and reapplied or starch poultices used for a few days before the tar is reapplied. A 1 per cent ammoniated mercury or ichthyol paste is used as a final medication.

Innoton ointment is also useful in cases which present a limited number of recurring pustules with no evidence of dermatitis. Its sphere of usefulness is, however, limited to folliculitis of the beard region (sycosis).

Temporary epilation by x-ray irradiation is helpful although its use is limited to sycosis. Epilation may be produced by a single dose or by an appropriate number of fractional doses. The x-rays have an unquestionable therapeutic action apart from actual epilation, an advantageous effect useful for treating any area. Small doses of x-rays reduce the infiltration, and probably exercise a partial bactericidal action on infecting organisms so that surface contamination is reduced. Attempts to eradicate the disease by internal measures are for the most part useless

The time required to cure a case by these methods varies with the extent of the disease, its duration, and the degree of skin tolerance to the remedies used. Perhaps from 3 to 6 weeks would be a safe estimate for the average patient when x-rays are used. The condition is unfortunately rebellious to all forms of therapeutic measures for long periods in a small percentage of patients.

The starch and sugar contents of the diet are reduced in every case.

A liberal supply of vitamins is assured. Yeast is an excellent source of vitamins used as a general tonic is furunculosis. It should, however, be fresh. Brewer's yeast is preferable in this case. Vaccines have been used despite the fact that they are of little value in superficial folliculitis. A stock vaccine is made from the various strains of staphylococcus peculiar to the district in which the patient

lives. This vaccine is probably as good as, or better than, an autogenous vaccine. The dosage ranges from 50 million to 500 million given over a course of 6 weekly injections. *Manganese* is useful although not reliable. Its use brings about definite pain.

Impetigo Neonatorum (Pemphigus Neonatorum)

Impetigo neonatorum is a bullous eruption presenting the features of a widespread attack of impetigo contagiosa. The staphylococcus is the causative organism The condition occurs at intervals in epidemic form in institutions The infection is not free from danger, usually attacking an adult suffering from impetigo contagiosa It is very difficult to control an epidemic once it starts. The malady spreads from infant to infant in a mysterious way despite the painstaking and exhaustive precautions taken to control it. The mortality varies greatly with various epidemics A 50 per cent mortality or more is not an unusual figure The lesions are bullous. Large raw areas are exposed as a result of rupture and coalescence of the bullae

Treatment—The eruption becomes so widespread that the use of starch poultices is valueless. The treatment is further complicated by the fact that the standby treatment for impetigo of a 1 per cent ammoniated mercury paste is not well tolerated and, in fact, aggravates the condition in the majority of cases. Bullae are evacuated by snipping. The daily use of an antiseptic bath containing potassium permanganate or boracic acid is beneficial The entire body surface is then painted after the bath with a 2 per cent aqueous solution of gentian violet. Gentian violet should further be repeatedly dabbed on the raw areas from which it may tend to

be wiped out by the continued exudation accompanying this condition.

A 5 per cent aqueous solution of silver nitrate, repeatedly dabbed on the whole surface of the body until a black coagulum is formed, is another serviceable medication. Splinting of the arms and legs may be necessary to prevent spreading the infection through contact and scratching Cases of impetigo contagiosa should without exception be completely isolated and the place of outbreak, which may be in an institution, adequately quarantined and disinfected.

Granuloma Pyogenicum

Granuloma pyogenicum is a red tumor-like growth which is small and rounded with a constricted base. The condition is bright red in color and develops for no apparent cause at the site of a minor injury. It consists of exuberant granulation tissue covered with delicate epithelial cells which give the surface a milky white appearance. The mass appears to arise in connection with a cutaneous vessel similar to a spider angioma. Staphylococcus can be isolated from it, but the staphylococcus is unquestionably a secondary invader despite the fact that it has been isolated from the lesion.

The treatment of granuloma consists of application of *carbon dioxide snow* or destruction by *electrocoagulation*.

INFECTIVITY OF SALIVA IN EARLY SYPHILIS

Usually, syphilis is acquired through direct contact with infectious lesions. Infection may take place, however, even in the absence of demonstrable lesions Particularly in the early stages of syphilis. the *Treponema pallidum* has been shown to be present in the blood, urine, cere-

brospinal fluid, and occasionally in the milk.

The secretion that is most often spread from 1 individual to others is saliva. It may be transferred directly by kissing, or indirectly through droplets or by the contamination of eating utensils. The frequency of primary lesions in and about the mouth indicates the importance of saliva as a factor in the dissemination of syphilis. Although saliva has been shown to contain Treponema pallidum, in the absence of lesions in the mouth its infectiousness has not been proved. If saliva itself were infectious its importance as a factor in transmission undoubtedly would be greater than if the infectiousness were due solely to contamination from sporadic oral lesions

Saliva was obtained from patients with untreated secondary syphilis, as it was felt that during this stage it would be most likely to contain Treponema pallıdum In none of the patients were there visible lesions about the parotid duct, although in 2 there were mucous patches elsewhere in the mouth saliva obtained from each patient was injected into 2 rabbits in amounts of 1 cc. into each testis Saliva from 7 patients was used. Two specimens were exammed by the darkfield method and both were negative In 3 cases, 1 of the moculated animals died within 8 weeks. The others were observed from 18 to 45 Each animal was examined at frequent intervals during the period of observation, and in no instance was there any evidence of syphilis found. In 5 of the experiments popliteal lymph nodes from 7 animals were inserted into the scrotal sac of 11 other rabbits node transfers were made from 12 to 23 weeks after the initial inoculation were negative after periods of observation ranging from 17 to 40 weeks. These results indicate that the infectiousness of saliva is due to the presence of syphilitic lesions within the mouth.

SKIN DISEASES OF THE HANDS AND FEET

Ringworm

Ringworm of the toes is the first of importance of local infections of the hands and feet. So universal is this type of infection, more especially between the little and fourth toes, that only very few practitioners cannot number among their patients 1 or more victims of this prevalent scourge. The condition appears to be more prevalent in the United States. The investigations of the University of California have shown that over 50 per cent of the newly matriculated male students presented at least clinical evidences of the disease As early 1892. Dielaleddin-Moukhtar adequately described the condition and its parasitic nature in his communication to the French Dermatological Society despite the fact that the malady appears to be of more recent discovery.

The infection is clinically recognized by the presence of white macerated skin between the fourth and fifth toes when it is limited to this area or it may involve the entire interdigital spaces and extend beyond them to the soles. Vesicular patches may occasionally appear on the soles or the toes, making the neighboring skin edematous and eczematous Very often, the nails are infected and assume a brittle, opaque and deformed appearance This diagnosis is confirmed by the histopathology which reveals the mycelium in preparations made directly from scrapings macerated in liquor po-The moist skin of the toes aftassae fords a suitable culture medium for the skin monilias. This infective process is frequently described as eczematoid ring-

worm which is an appropriate descriptive term of the combination of an eczema superimposed on primary ringworm infection of the feet.

It is important to take into consideration the extent of the eczema and the stage of infection by the ringworm. It is best to begin treatment for eczema, when eczema predominates, deferring applications of fungicides to a later stage of the disease. This procedure of treatment will readily clear up the pathology, thus showing that the whole process is primarily eczematous with the superimposition of secondary invasion by monilia.

Whenever ringworm infection is the predominating symptom the treatment is directed to destruction of the active parasites by removing the sodden masses of Reinfection from infected socks, stockings and shoes by disinfection with formalin, is also prevented. So wide is the selection of medicaments that it may be suspected that none of these therapeutic agents is satisfactory well-known Whitfield's ointment or its modification (15 grains benzoic acid, 15 grains salicylic acid and vaseline to make an ounce) remains the best fungicide despite the many medicaments recognized as fungicides Castellani's basic fuchsin paint is very useful. The involved patches between the toes are painted with 1 per cent silver nitrate in sweet spirit of niter and a simple paste in some ınstances

Dysidrosis

Dysidrosis is characterized by a series of cutaneous eruptions consisting of deeply seated vesicles on the palms and fingers simulating boiled sago grains. The feet and hands may be involved separately or together. The vesicular lesions do not rupture, but dry up and produce secondary exfoliation of the skin.

The lesions may, on the other hand, fuse to form blisters. Secondary infection occurs in some cases. Lymphangitis may occasionally be present. The warm weather favors the development of vesicular eruptions and in this way seasonal recurrences are relatively common. Endogenous and exogenous factors should be taken into consideration whenever an attempt is made to explore the possible causes of dysidrosis.

There appears to be a conflict of evidence in the etiology of dysidrosis without another parallel in medicine Eruptions may follow contact with certain irritants as in some forms of occupational dermatitis. They may also be the expression of an unknown endogenous and familial influence as outlined by Mc-Lachlan and Brown in 17 per cent of their cases Lesions of dysidrosis have also been produced by the ingestion of articles of food and the ingestion or application of certain medicaments, such as salicylic acid and belladonna. The present trend of thought enters around the relationship of dysidrosis to ringworm In 1919, Darier was of the opinion that after excluding exogenous dermatitis, dysidrosis was probably always due to direct fungous infection. This view is completely contradictory to the researches of Muende at St John's Hospital Muende never recovered or grew fungus from vesicles

An endeavor should be made to determine the exciting cause including possible external agents, such as articles of food, drugs, or ringworm infection of the feet. Since the time of Hutchinson, English dermatologists have recognized a "nervous factor." This "nervous factor" cannot easily be translated into suitable words. Worry and overwork may in this fashion have a share in provoking the disease.

Erysipeloid

In 1873, Baker first described erysipeloid and named it "erythema serpens." Fifteen years later Rosenbach offered the medical profession his classical contribution on erysipeloid. Bedford of Leeds has justly stated that most general practitioners of experience are familiar with the disease despite the fact that it is not known to them by a specific name. Most cases occur among cooks and fishmongers. Infection usually follows the prick of a bone when handling fish or game. The offending microorganism is identical to that producing swine erysipelas. The incubation period averages 5 days. The infected finger becomes stiff, itchy. swollen, and a sharply defined bluish-red zone extends distal to the wrist and very rarely spreads beyond it. The accompanying constitutional disturbance is usually slight despite the very alarming appearance of the disease and its exaggerated subjective signs. Mild cases last about 3 weeks There is, however, a tendency to relapse. Symptoms are invariably aggravated by using fomentations in an effort to bring about some relief. Good results follow applications of 40 per cent ichthyol in vaseline.

Generalized Skin Diseases Affecting the Hands and Feet

Lichen planus and psoriusis are among the dermatologic lesions which attack the hands and feet. Psoriatic involvement of the hands is, however, very exceptional. The diagnosis of these conditions is established by the presence of characteristic eruptions of these 2 diseases elsewhere on the body.

Eczema of the hands is identical to eczematous lesions elsewhere on the body but in itself it possesses certain distinctive features which merit their consideration as a separate entity. Involvement of the hands in eczema may occur in any

advanced case of eczema. Its distribution on the hands, more especially when it begins or becomes confined to the dorsum of the hands, suggests the influence of an external irritant. This feature is one of the most significant diagnostic signs in industrial dermatitis. Confronted with eruptions in this situation the practitioner should differentiate between idiopathic eczema and contact dermatitis. Hypersensitivity is confirmed by a positive patch test which will invoke the appearance of lesions whenever the patient contacts with it.

The treatment of eczema is identical to the treatment of the disease elsewhere on the body. The eminent French dermatologist, Jean Darier, has justly stated that "the therapy of eczema should be symptomatic and opportunist rather than systematized and preconceived." There is no formula for satisfying all requirements in all circumstances. Treatment should vary with the changing phases and it may be deemed necessary to treat different eczematous areas in the same patient in different ways. Evaporating lotions, such as lead-glycerin or calamine lotion, are applied on acutely congested and inflamed eczematous areas. Oily calamine lotion is recommended for dry eruptions Subacute eczema is better treated by a soothing, protective paste. Chronic, dry and rebellious eruptions are treated by stimulating applications. Coal tar in paste form or in ointment base is usually the most serviceable stimulating application. Roentgenray irradiation is the most serviceable regimen of treatment for chronic eczema of the hands.

Skin Diseases Localized to the Hands and Feet

Among the skin diseases localized to the hands and feet the following conditions ment consideration *Acroderma*-

titis perstans (continua) is included by some dermatologists among the rarer diseases. The disease has been ascribed to some infection with a strain of virulent staphylococcus possessing an elective affinity for the extremities, or to an allergic reaction of the individual to the staphylococcus. The clinical picture is characterized by the appearance of a red scaly patch on the hands or feet. The palmar and plantar surfaces as well as the instep are sites of election. The eruption may be limited to 1 foot or hand or may begin on 1 extremity before extending to the other limb.

Crocker introduced the term "dermatitis repens" to identify acrodermatitis perstans affecting only the thumb, I finger, or I toe In this case the nail is usually affected. Abortive forms of "dermatitis repens" are met with in which only small pustules resembling dysidrosis are present. It is identified by the rebellious nature of eruptions. The appearance suggests ringworm infection. Microscopic examination of pustules always reveals a negative culture. The disease follows a prolonged course.

Crude coal tar in the proportion of 60 minims to the ounce (4 cc to 30 cc), dissolved in acetone or incorporated in a paste is beneficial. The curative effect of these applications is enhanced by repeated small doses of x-rays given within the limits of safety. Sutton recommends Ruggles' mixture (1 part salicylic acid, 5 parts tannic acid and 50 parts alcohol) which is painted on once a day. Pustules are opened and cleaned out as a preliminary treatment. Autogenous vaccines and the irradication of foci of infection have been advocated by clinicians supporting the view that the disease is infectious.

Chilblains are dark red, slightly raised, itchy swellings well known to all clinicians

Lupus erythematosus of the hands bears some resemblance to chilblains. It is distinguished from chilblains by its persistence throughout the summer months and by the associated eruption on the nose and cheeks. Only in very exceptional cases is lupus erythematosus confined to the fingers alone. Chilblains are occasionally met with in delicate persons and in individuals exhibiting acro-asphyxia. The red, congested state of the extremities is popularly ascribed in these people to a "bad circulation" The victims are usually robust, healthy children or adolescents. This fact makes it difficult to accept unreservedly a tuberculous or special chilblain diathesis, or even focal infection as causal factors.

The administration of thyroid or calcium has been beneficial to some patients but these preparations and other drugs have in general proved disappointing The local applications advised include tincture of iodine, friction with camphorated alcohol, ichthyol pastes, and immersing the hands for 15 minutes, twice daily, in a solution of peroxide of hydrogen (6 volumes). The solution of hydrogen peroxide is perhaps the best medication. Small doses of x-rays have been recommended. These are given before the onset of the cold weather and repeated in 3 weeks' time. This treatment is useful as a prophylactic measure in individuals predisposed to seasonal Roentgen-ray therapy should only be given by the dermatologist experienced with the x-rays.

Warts are simple epitheliomas produced by a filtrable virus. Warts have been made to disappear by mere suggestion. The late Professor Bloch of Zurich, whose scientific achievements in dermatology are recognized, practiced this form of esoteric therapy and obtained success among 55 per cent of his patients. In 1936, Goldsmith gave a full

account of Bloch's procedure and of which the following summary is submitted.

The blindfolded patient rests his hands on a pantostat. The motor is started to produce an effect. The warts are colored. The patient is then told not to wash off the paint, and that the warts will disappear. Swelling of the wart or possibly a slight hemorrhage into the wart substance often followed this method of treatment. The warts disappear within 2 months in successful cases.

Professor Bloch's suggestion therapy for removing warts may perhaps be regarded as an illustration of the effect of mind over matter despite its restricted application It is a clinical fact to be accepted as such until the ripened knowledge of biochemical science reveals its more precise scientific significance. Clinicians gifted with the ability to put this suggestive therapy into practice, as the wart charmers are doing in country districts, may prefer to use it. The accepted technic for removing warts includes destructive chemical applications such as trichloracetic acid or refrigeration with the carbon dioxide pencil. Scrubbing the hands with Fels naptha soap has been advised as a simple and expeditious plan for treating a group of The most difficult of all small warts warts to remove is the painful plantar wart which, aside from the discomfort it brings, is more than a minor cosmetic problem The curette, surgical excision, or radium may be employed for removing plantar warts. A relatively simple plan for removing these warts consists of applying a 20 per cent salicylic acid plaster cut so exactly as to cover the wart completely kept in place by a larger piece of adhesive plaster for 24 hours. The dressing is removed and plaster bandage alone is then applied for 2 or 3 days This procedure is repeated with longer applications of the salicylic acid plaster according to the reaction. As the wart softens, it is scraped away from time to time with a blunt knife or a curette. Plantar warts may be obliterated within 4 or 6 weeks by this plan provided the details are scrupulously observed.

INTRACTABLE URTICARIA

Management — Urticaria (hives) is often a difficult problem to the general practitioner and specialist. Angioneurotic edema may be the cause of death. Attacks are usually self limited and easily controlled by abstinence from foods to which the patient is allergic. The condition can also be controlled by cathartics, alkalis, and the administration of calcium by mouth, and by employing epinephrine or ephedrin. These prophylactic measures are occasionally valueless and in these instances the nervous or psychic element may be so pronounced as to demand psychotherapy. Bacteriologic study and treatment of infection have occasionally been successful.

Allergens producing urticaria enter through the intestinal tract. Cutaneous tests are usually negative.

Most clinicians agree that bacterial allergy exists, but the available cutaneous tests with bacterial products to determine the causes of hypersensitiveness, except for tuberculosis, are valueless. It is possible to isolate an occasional colony of indifferent or green streptococci from the colon of a normal individual. The presence of these bacteria in abundance or a positive test for hemolytic staphylococci from the wall of the colon is definitely abnormal.

Traub treated 4 cases with *vaccines* of rectal streptococci with good results

The vaccines of green and indifferent streptococci may be given in doses starting with 1,000,000 bacteria and doubled every 4 days. Vaccines of hemolytic streptococci should be given in doses starting with 10,000 bacteria. The next dose is halved if a decided local reaction occurs.

Bacteriologic studies of the stools in cases of urticaria or angioneurotic edema should be made.

The use of foreign proteins as prepared from milk are contraindicated because of the danger of patients becoming hypersensitive to this common food

PERMEABILITY AND ABSORPTIVITY OF THE SKIN

The permeability and absorptivity of the skin are of particular importance to the dermatologist and general practitioner on account of the systemic and local effects of the cutaneous medication.

Mussey proved in 1809 that after topical applications of certain drugs to the unbroken skin the drugs applied were present in the urine. Reilly reported in 1901 therapeutic results after cutaneous applications of such substances as belladonna, mercury, pilocarpine and codliver oil. He also called attention to the presence of salicylic acid, turpentine, guiacol, creosote and phenol in the urines of individuals treated with these preparations.

Substances soluble in oil are more readily absorbed through the unbroken skin than those soluble in water.

Zondek reported that drugs soluble in such preparations as alcohol, ether, benzine and chloroform are more rapidly absorbed in greater amounts than those incorporated in only bases. He also reported that alcoholic solutions of estrogenic substances are percutaneously ab-

sorbed more rapidly than those in oily vehicles

Macht found that most essential or volatile oils, such as cinnamon, wintergreen, cloves, peppermint, lemon and orange, are readily absorbed through the unbroken and normal skin. He reported the death of animals following the cutaneous absorption of these substances.

Other investigators reported poisoning and death following the absorption of salicylic acid, and phenol through the skin. Caution should be exercised in the use of phenol since it is often used in "skin peeling" preparations

"Bleach creams" and "freckle removers" containing mercury salts are also dangerous on account of the possible absorption of this metal.

Various investigators have reported the cure of rickets in animals and in humans from cutaneous applications of cod-liver oil or ointments containing irradiated cholesterol Recovery is due to the absorption of vitamin D Vitamin C is also absorbed percutaneously as evidenced by the increased amount in human milk after the applications of ascorbic acid solutions to the intact skin of mammals

Baer applied to the skin of spayed rats estrogenic substances contained in hydrous wool fat, or petroleum or olive oil. He obtained no appreciable difference in the time required for estrus to develop irrespective of the vehicle used. He further concluded that the follicular hormone is not stored in the skin since a minimal dose was necessary to maintain estrus.

MacBryde treated women suffering from hypogonadism and lack of mammary development with injections of 5000 international units per gram of estradiol or estradiol benzoate. When these injections were discontinued a rapid regression in the size of the breast was

observed. When the breasts had returned to approximately their original size, a daily unilateral application of 5 Gm. of the estrogenic ointment was made. The other breast was anointed with the same quantity of the vehicle. The latter breast revealed a slight enlargement. while the breast treated with estrogen showed a decided increase in size and progressive growth which was maintained throughout the treatment. There were also evidences of an active estrous state by enlargement of the uterus and relief of the hypogonadal symptoms. The results obtained from a comparative study of these 2 forms of therapy were decidedly in favor of inunction.

Eller and Wolff offer the following conclusions:

- 1. Medicaments applied to the unbroken skin may be absorbed into the blood stream.
- 2. The rate of absorption may be influenced by the vehicle as well as by the drug it contains.
- 3. Volatile substances such as alcohol, ether and benzine are vehicles with a much higher rate of absorption than fats.

From percutaneous experiments it appears that:

- 1 Fats permeate the skin and do so in a large measure along the hair shafts and into the sebaceous gland ducts.
- 2 Liquid fats permeate the skin more rapidly than solid fats
- 3 Animal fats show the greatest depth of penetration with vegetable fats next and mineral oils last
- 4 Most of the fats show optimum penetration between 4 and 6 hours after application. After 6 hours, the quantity of fat in the deeper tissues appears to diminish.

CHANGES IN THE NAILS AS AN AID TO DIAGNOSIS AND PROGNOSIS

Few medical men, when examining a patient, make even a cursory inspection of the nails Yet a good deal of informa-

tion can sometimes be obtained from these structures. Like every other organ their normal growth depends upon the general health. When all the nails of the hands and feet show the same alteration, the presumption is that it is due either to a congenital anomaly or, in the absence of any adjacent skin inflammation, to some general condition affecting all the nails. When only a few of the nails are affected, a local cause should be sought, such as a recent or remote injury, an infection of the nail itself (as in ringworm) or an inflammation or growth affecting the skin or deeper tissues around the nail. Admittedly, changes in the nails are not always of first class importance but these changes may be very helpful in giving support to a diagnosis which is otherwise doubtful. If nails are affected in any general condition, it indicates its severity and influences the prognosis

Color of the Nails-One of the first things to be noted is the color of the nails. This depends somewhat on the climate. Pressure on the nail drives the blood from the nail bed and when the pressure is removed, the rate with which the blood returns is an index of the vigor of the circulation. The commonest alteration in color is found in leukonychia. Everyone is quite familiar with the white spots which appear from time to time in the nails. They may be punctate or arranged in transverse striae, but there are also rare cases in which the nails are completely white and look as if they had been painted with white paint. This condition has been known to appear in individuals who were apparently perfectly normal otherwise. Some of the cases have a family history of the condition, but it has been known to develop when there are trophic nerve disturbances, such as occur in nerve leprosy The small punctate and striate lesions are

comparatively common and are generally supposed to be due to trauma. In the striate form, the white areas run transversely across the nails, which may show more than 1 of these lines. They are much more frequent in women than in men; this is probably due to improper manicuring. Althausen and Gunther have reported the presence of white transverse bands in the nails of the fingers and toes and regard it as a sign of acute or chronic arsenical poisoning. In chronic arsenical poisoning, there is a concentration of arsenic in the hair and nails By chemical analysis of pieces of the nails and hairs, the poison can be determined Similar white bands on the nails have also resulted from the oral use of thallium acetate.

The white color is usually attributed to the presence of air spaces in the nail due to an injury which separates the layers of the nail substance. Singer has recently suggested that they are due to imperfect keratinization of the growing nail matrix resulting from hypothyroidism.

The nails may show discolorations varying from light yellowish-brown to blue, purple and black. In chronic arsenical poisoning, instead of leukonychia the nails may show the same brown pigmentation as the skin of the fingers or toes. In Addison's disease, the nails are occasionally pigmented. A single longitudinal brown band is usually due to a pigmented naevus in the nail matrix

The slate-blue discoloration of the skin in argyria, usually most marked on the exposed parts, is very disfiguring. It is due to the deposit of metallic silver in the epidermis and true skin. The same discoloration occurs in the nail beds and may be the earliest manifestation of argyria

In cases of chronic mercurial poisoning, a brownish-black discoloration, much

darker than in argyria, may occur. It is due to the formation of sulfide of mercury in the tissues. A blue-black discoloration of the nails due to hemorrhage under them is very common. It is most often due to an injury, but in bleeding diseases, such as purpura, hemophilia and scurvy, spontaneous hemorrhages may occur under the nails, and in these cases they usually occur under several of the nails. In tabes dorsalis, hemorrhages may suddenly appear in all the nails of the toes. Hemorrhages under the nails, preceded by neuralgic pains, may also occur in diabetes.

A jet black discoloration of the nail occurs in diabetic and other forms of gangrene.

Changes in Shape—Apart from any alteration in color, the nails may become altered in shape and size. Clubbing of the fingers and toes in chronic pulmonary and cardiac conditions is well known, and when that occurs the nails become curved from above downward and from side to The opposite condition also occurs, in which case the nails are either flat or concave, producing what is known as spoon-nail (koilonychia). The nail plate is concave instead of convex surface of the nail is usually smooth, but some degree of longitudinal thickening may be present. All the nails may be affected, or the anomaly may be limited to the thumbs and forefingers. In patients who suffer from alopecia areata a flattening or slight concavity of the nails of the forefingers and occasionally of the middle fingers and thumbs is very com-The cause of spoon-nail is not known It may occur in association with nutritional anemias or nervous diseases

Fragility and Splitting — This is another fairly common condition. Some persons are born with nails which are brittle and tend to split and break off at the free ends. A similar condition

may also be acquired by prolonged contact with chemicals, particularly alkalis. By too frequent manicuring or the application of chemicals to remove colored nail enamels, a softening and splitting of the nails may result. There is also the condition known as eggshell nail in which the nail plate is soft, semitransparent, bends easily and splits at the end. This particular change has been reported in association with arthritis, peripheral neuritis, leprosy, and hemiplegia. A somewhat similar condition may occur in late syphilis, producing onychia syphilitica sicca. In this condition, all the nails are affected. They are dry, atrophic and tend to split. It may be the only objective sign of syphilis.

The use of sulfur is advised in all atrophic conditions of the nails.

Lines on the Nails-Longitudinal striation of the nails is a very common condition in adults past middle life. In slight cases it is merely an exaggeration of the normal longitudinal ridges of the nail bed, but in well-marked cases it is accompanied by splitting of the nails (onychorrhexis) at the free margins. It is common in persons who have a focus of infection at the root of a tooth or in It also occurs in gout and nervous diseases, such as neuritis, hemiplegia, and myxedema Dryness of the skin, with lusterless nails showing longitudinal or transverse lining is also seen in cases of vitamin A. B. and D defi-Administration of the appropriate vitamins in these cases will restore the nails to normal Microscopic exammation of pieces of the splitting nail will differentiate the condition from ringworm

There is also a rare congenital family defect of the nails in which all the nails of the hands and feet show an atrophic condition with a definite raised longitudinal ridge running down the center of

each nail. It looks as if each nail had been gripped with a pair of forceps and squeezed so as to make the center rise up into a ridge. This condition, curiously enough, is always accompanied by complete absence or extreme smallness of the patellae. Why this should be and what the connection is between the nails and patellae are not known.

Almost as common as longitudinal lines of the nails are transverse lines. usually known as Beau's lines. They appear on the nails as a result of previous interference with the growth of the nail matrix. They consist of a superficial depression running across each nail These lines may be due to a local cause, in which case all the nails are not usually affected, or to some general disturbance in which all the nails of the hands and feet are equally affected. The local causes are inflammatory lesions in the region of the growing nail matrix as in eczema, psoriasis, general exfoliative dermatitis (especially after the administration of arsphenamine preparations), paronychia, and trauma. Of the general causes, the commonest are acute infections, such as erysipelas, influenza, pneumonia, scarlet fever, measles, and typhoid fever: but any condition in which the general vitality is temporarily lowered, such as from loss of blood, prolonged and severe seasickness, nerve shocks, epileptic attacks, exophthalmic goiter, and diabetes, cause Beau's lines to appear When the causative factor is repeated, a succession of these lines may result and the distal part of the nail may become loose and drop off.

Shedding and Atrophy—Shedding of the nails without any previous alteration in them or in the skin around them may also occur. Certain individuals shed their nails regularly once a year for no apparent reason. Many of these cases have a family history of this peculiarity.

In epidermolysis bullosa, in which trivial injuries give rise to the formation of large blisters in the skin, the nails frequently fall off. The nails may also be shed after fevers, especially scarlet fever, in tabes dorsalis, and in diabetes. In extensive skin diseases, such as exfoliative dermatiti, pemphigus foliaceus, extensive eczema, and alopecia areata, a similar loosening and shedding of the nails is apt to occur. In all these conditions the nails grow again.

Another frequent change in the nails is atrophy. The nails become small and misshapen, so that only a deformed or thinned stub is left to represent them Some degree of atrophy is nearly always present in the nails of the third, fourth, and fifth toes This is probably due to the constant wearing of shoes. Atrophic nails may be congenital. It is usually associated with other ectodermic defects. such as extreme thinness or absence of the nails This change in the nails is frequently seen in mentally defective children It may also be an acquired condition and may follow injuries, scars, frostbite, sclerodactylia, Raynaud's disease, radiodermatitis, and syphilis also occurs in hyperthyroidism, exophthalmic goiter, injuries, leprosy, tabes dorsalis, syringomyelia and in prolonged debilitating diseases. Another of the rarer causes is tetany following destruction or extirpation of the parathyroids Atrophy of the nails is permanent

In cases of nail-biting, the nails may be so bitten down that they look small and atrophic. The skin around them is often swollen and inflamed so that the nails appear to be sunk below the normal level and look smaller than they really are. There is also another condition allied to nail biting which is usually seen in adults of nervous temperament. These persons are constantly picking at the free edges of their nails, so that small

pieces become chipped off, making the nails much shorter than normal. In all prolonged itchy skin diseases, such as chronic eczema and neurodermtaitis, the nails of the fingers may be worn down at the tips to a straight line or even show concavity. This is due to the constant scratching.

Thickening and Hypertrophy—The last condition which must be mentioned as of diagnostic value is a thickening and hypertrophy of the nails. It occurs in 4 forms: (1) Simple thickening of the nail substance; (2) subungual hyperkeratosis, (3) thickening in chronic nail inflammations, and (4) onychogryposis.

In simple thickening, the nails become thicker toward the free ends so that a very hard horny peg, greenish or blackish in color, is produced. The surface of the nail is smooth and regular or only slightly longitudinally lined. Congenital cases of this condition have been recorded, but in chronic eczema with hyperkeratosis of the palms and soles this nail change is not infrequently seen.

In subungual hyperkeratosis, a horny mass grows from the nail bed and pushes up the overlying nail plate. This condition usually accompanies a chronic skin disease, such as eczema and psoriasis. Chronic arsenic poisoning and general paralysis may also be causative of this condition The condition must not be confused with yeast infections under the nails, in which the nail always has a dark greenish or bluish color and the material which can be scooped out from under the nail is much softer than in hyperkeratosis Examination microscopically and by culture will also show the presence of yeasts.

In all chronic inflammations of the nail bed and infections of the nail folds there is an overgrowth of the nail substance so that the nail becomes considerably hypertrophied. This usually occurs irregularly, producing nodular thickenings of the nails. It is seen in ringworm of the nails and in all types of paronychia. Its treatment is that of the condition causing it.

Of all the hypertrophies of the nail one of the commonest and most striking is onychogryposis. It may affect all or only a few of the nails. In nearly all cases it is limited to the toenails and is especially apt to affect the nail of the great toe. Whenever it occurs on the fingernails, the practitioner should always eliminate syphilis. The nail becomes greatly overgrown and irregularly thickened in onychogryposis. It is usually of a brownish, greenish, or blackish color and as it grows it becomes curved like an animal's horn. It is so hard that the patient cannot cut it. It is often seen in elderly persons and may be associated with deformities of the toes, especially hallux valgus. It has been noted in association with peripheral neuritis, leprosy, tabes, and hemiplegia. Pituitary and thyroid dysfunction are occasionally causative of it, but in the majority of cases it is the result of neglect and want of cleanliness.

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DIETOTHERAPY

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Advances in Dietetics — John D. Comrie¹ discusses advances in nutrition He says that Caloric requirement figures were set too high in the past, and there is no need for such overnourishment. He suggests an allowance of 2400 Calories for a normal adult. The tendency to eat too many Calories, and not enough of the foods containing minerals and vitamins is too prevalent. He calls attention to the use of skimmed milk by the poor who cannot afford to buy whole milk, and the return to the use of less refined foods, such as whole-meal

One hundred and twenty grams of carbohydrate are suggested as a sensible intake for the obese, with 70 Gm of protein and only 2 pints of fluid to be included daily. The diet should be restricted to 1000 or 1200 Calories daily while the patient is in bed, and 1500 Calories when he returns to work. Sugar and sugar-containing articles such as jam, preserved fruits, sweet cake, and candy are prohibited, as well as fried foods, high fat meats, such as bacon, pork, duck, and goose, sauces thickened with flour, beer, stout, and sweet aerated waters. He suggests the use of clear soups, meat extracts, calves' foot jelly, diabetic jams without sugar, and mayonnaise made from mineral oil

Dunlop has recommended a diet providing 1000 Calories, containing 100 Gm of carbohydrate, 60 Gm of protein, and 40 Gm of fat

Breakfast—Orange or ½ grapefruit without sugar; wholemeal bread, 1 oz (1 thin slice); or 2 pieces of ryvita or vita-weat; butter, ¼ oz.; 1 egg, or 1 oz. lean cold boiled ham or tongue; tea or coffee with milk.

DINNER—Clear soup, or marmite, or oxo, if desired; a medium helping (2 to 3 oz.) of cooked lean meat, chicken, rabbit, tripe or white fish (if fish is taken, ¼ oz—butter may be used for cooking); a large helping of vegetables, 1 apple, or pear, or other fruit

TEA—One egg, or ¾ oz cheese, or medium helping of white fish, lean meat, chicken, or 1 oz cooked lean ham or tongue; fresh salad or tomato, wholemeal bread, 1 oz; butter. ¼ oz., tea or coffee with milk.

Supper—Wholemeal bread, 1 oz., or 2 pieces of ryvita or vita-wheat, or 3 water biscuits, butter, ¼ oz, skim milk, coffee, if desired; 1 medium sized orange.

Daily ration of skim milk, ½ pint, saccharin may be used for sweetening, water, 2 pints

To increase this diet to 1100 Calories give whole milk in place of skim milk

To increase further to 1200 Calories add 14 oz butter

The diet for nephritis which he recommends follows: (It is the diet used by Cameron, who believes in the use of milk to provide the tissues with the essential amino acids, thereby preventing a breakdown and lowering of resistance to infection)

8 A M, 5 oz milk, 10 v M, 5 oz glucose fruit juice mixture, 12 NOON, 5 oz milk, 2 P M, 5 oz glucose fruit juice mixture, 4 P M, 5 oz milk, 6 P M, 5 oz glucose fruit juice mixture, 8 P M, 5 oz milk, during the night, 5 oz glucose fruit juice mixture

The glucose fruit juice mixture is 30 per cent solution of glucose in water with the juice of 1 or 2 oranges or lemons added to each pint for flavoring purposes

As the patient improves, more protein may be added and bread and butter, Benger's food, arrowroot or other light cereal may be added. He uses the concentration of urea in the urine as a guide to the protein intake. When the maximum reaches 1.5 and 2 per cent, 50 Gm of protein may be taken; at 2.5 per cent

he raises it to 75 Gm. daily, and if it rises to 3.5 per cent, 120 Gm. of protein may be permissible

High protein diets in edema and albuminuria have been generally accepted Following is one which is given by Dr. Comrie. It contains 2500 Calories and contains 100 Gm of protein, the greater part of it being in the form of complete proteins.

Breakfast—Milk, 1 pint, bread, 4 oz Lunch—Milk, ½ pint

DINNER—Boiled rice, sago, arrowroot or cornflour, 2 oz, milk, 1 pint; bread, 6 oz. Supper—Milk, 1 pint, bread, 4 oz

The following is another high protein diet providing 2000 to 2300 Calories and contains 100 Gm. of protein:

Breakfast—Weak tea, bread, 6 oz; butter, ½ oz, porridge and ½ pint milk, if desired Lunch—Milk, ½ pint, bread, 1 oz

Tea—Weak tea, bread, 6 oz, butter, ½ oz Dinner—Fish or chicken or lean meat, 6 oz, vegetables, 8 oz, bread, 4 oz

When symptoms of uremia threaten, it is well to reduce the protein. The following diet supplies about 2000 Calories and contains some 40 Gm protein. The foods are basic in reaction.

Breakfast—One glass orange juice, baked apple with cream, 2 oz, bacon, 2 oz, $\frac{1}{2}$ slice toast with butter, milk, $\frac{1}{2}$ pint

Lunch—One glass orange juice, baked potato with butter, salad; ½ slice bread, milk, ½ pint, melon or other fresh fruit

DINNER—One glass orange juice; vegetable cream soup, potatoes with peas and carrots, buttered, ½ slice bread, fruit salad

The diet which he gives for diabetes is as follows:

It provides 2000 Calories and contains 130 Gm carbohydrate, 80 Gm protein and 135 Gm of fat.

Vegetables, 17 oz , orange, $3\frac{1}{2}$ oz , milk, 10 oz , brown bread, 6 oz., lean meat, 2 oz., bacon, $1\frac{1}{2}$ oz , cheese, $\frac{3}{4}$ oz , 3 eggs , butter, $2\frac{1}{2}$ oz

For hematemesis caused by hemorrhage from acute gastric ulcer, he recommends

the treatment used by Meulengracht (1935). A puree diet is administered together with an alkaline mixture containing sodium bicarbonate, magnesium carbonate, and extract of hyoscyamus.

The diet begins in the morning at 6 A M. with tea, white bread and butter; at 9 A. M oatmeal porridge with milk and bread and butter; at 1 P. M. dinner including such articles as meat balls, omelette, fish balls, mashed potatoes, vegetable purees, stewed fruit, gruel and pudding of rice or tapioca; at 3 P. M. cocoa; and at 6 P M white bread and butter, sliced meat, cheese and tea.

ANOREXIA NERVOSA

Psychoneurotic individuals very often complain of poor appetite and many of these patients because of their hypochondriacal ideas show many stages of malnutrition. In the psychoneurotic group, states E S. Cross,² a number of instances of almost complete anorexia is to be found and these present no organic lesions. The term anorexia nervosa has been applied to this condition.

In the treatment of anorexia nervosa, the principal and essential measures are rest, isolation, full feeding, and analysis of difficulties

The method of feeding these patients is very important. The alimentary processes are depleted because of long disuse and therefore food must be given in small quantities at first and increased gradually. If food is urged on the patient at first in too large amounts he will feel that he is asked to do the impossible and become frightened. One may first give 2 ounces of milk every 2 hours for 8 feedings on the first day, doubling the amount on the second day, and on the third day giving 6 ounces every 2 hours. Fruit juice may then be substituted for 1 or 2

feedings, or meat broth, if desired. On the fifth or sixth day, salty crackers, dry toast or thin bread and butter may be added to alternate feedings. Milk should be increased to about 2 quarts in 24 hours but part of it may be given as cream soup, custard, junket. Eggs may be added, also pureed vegetables, stewed and fresh fruits, chicken, fish, and meat until a normal diet is reached. "When a fair amount of mixed food can be taken at regular mealtimes it is a good plan to teach the patient to swallow 1 or 2 raw eggs after the solid food and milk have been taken." One must decide during this time whether it is advisable to give the patient food between meals or not. It is often possible to give some milk and crackers before bedtime.

THE DIABETIC CHILD

Waldo E. Nelson, M.D.,³ gives a splendid table of the essentials of diet which he thinks every diabetic child should have

TABLE I

ESSENTIALS OF DIET FOR DIABETIC CHILDREN

- 1 Sufficient Calories for growth and activity.
- 2 Adequate protein, minerals and vitamins.
- 3 Ketogenic-antiketogenic ratio of not more than 1.5.
 - 4. Adequate to satisfy appetite.
 - 5 Variation to avoid monotony.
- 6 Sufficient approximation of average diet to permit entire family's partaking of it.
- 7 Choice of foodstuffs compatible with financial status of family

Table 2 gives some "starting diets," as he calls them, on which the child should be put after he comes out of coma

After a child is started on his diet, Dr. Nelson suggests that the diet be constantly adjusted to meet the needs of the child for growth and activity, as well as appetite. Constant adjustment of

Number of		per lb.	Calories per lb	K/AK		
diet	Carb.	Prot.	Fat	body wt.		
1 2 3 4	2 3 3 3	1 0 1.5 1.0 1.5	2 0 1.5 1.5 1.0	30.0 31.5 29.5 27.0	0.8 0.6 0.5 0.4	

TABLE II
EXAMPLES OF STARTING DIETS

insulin is also necessary to prevent glycosuma and shocks.

When calculating the diet of the child, Dr. Nelson bases the number of Calories on the weight of the child calculated slightly less than the normal should be for the age and height of the child. He does not approve of starvation diets to determine the glucose tolerance He bases his starting diets on the following figures:

- 1 Approximately 32 to 27 Calories per pound of body weight for children 5 to 12 years of age
- 2 At least 1 Gm of protein per pound of body weight for young children and slightly less for the older child
- 3 Ketogenic—anti-ketogenic ratio of less than 15

The individual needs of the child cause many variations. Seldom, he says, do they give more than 220 Gm of carbohydrate. After a child has been on the diet for a certain length of time, adjustments are again made. Weight gain and satisfaction are given consideration.

If the gain in weight is satisfactory, but the appetite is not satisfied, then the bulk of the diet is increased without increasing the calories. On the other hand, the bulk may have to be decreased in order to get the child to eat everything. No proprietary diabetic foods are necessary. Insulin is adjusted until there is only a slight trace of sugar in the urine. Changes in activity, infections.

body growth may make it necessary to change the quantity of insulin. With increase in activity, the blood sugar goes down, if the proper amount of insulin has been given. If the child's blood sugar is very high, it may still go higher with increased exercise. Diabetic children should be instructed to carry lumps of sugar in a small metal box to take on feeling symptoms of shock.

Dr. Nelson has also observed that it is usually necessary to increase insulin at the opening of school and decrease it after school closes. If the child develops an infection, the following procedure may be followed during the acute stage.

- 1. Soft, easily digested diet
- 2 Carbohydrate maintained at essentially the level of the regular diet
 - 3. Moderate decrease of protein.
 - 4. Marked decrease of fat
 - 5. Increase of insulin as necessary

The free unrestricted diets which have been advocated in recent years are not approved by Dr Nelson His reasons for disapproval are:

- 1 Control of child's growth
- 2 Insurance of a balanced intake
- 3 Instruction of the child and his family in the content of an adequate diet
- 4. Proportionate distribution of the diet throughout the day
- 5 The psychologic effect of aiding in training the child in self-discipline

If the child is allowed to eat as he pleases, the result will not be favorable, because it has been found that the diabetic diet is a well balanced adequate diet, and seldom does the average housewife plan meals which are adequate. The instruction which goes with the diabetic diet is valuable for the entire family. After a diabetic child has grown into an adult, Dr. Nelson says that it may be possible for him to estimate rather than measure his diet because of years of training

^{*} Ketogenic-antiketogenic ratio.

FOOD SENSITIVENESS

Walter C. Alvarez⁴ presents 2 problems confronting the physician today concerning food sensitiveness. One is the problem of getting more physicians alert to the possibilities of the field, to watch for patients whose indigestion, headache, or mental attitude is due to eating rather than some other cause. The other problem is to keep other physicians from becoming too enthusiastic over food sensitiveness, thereby inflicting limited diets on patients and restricting them for such a long period of time that much weight is lost and other damage done. Dr Alvarez puts little stress on the skin test but does emphasize the diary method. Since distress usually follows soon after a food is eaten, it can be traced if the patient lists the foods eaten, especially the odd or unusual ones

If the distress of which the patient complains is present every day it may be difficult to determine which food it is by the above method. In this case he suggests the elimination method. He asks his patient to eat nothing but a few foods for 2 days An example is that he restricts the food to lamb, rice, butter, sugar, and canned pears. These foods seldom cause trouble even in highly sensitive people. To start off on a diet of milk and custard is very bad, since milk and eggs are very common offenders After the patient has remained on the few foods mentioned above. Dr. Alvarez adds such as gelatin, carrots, asparagus, string beans, rye krisp, arrowroot cookies, turnips, potatoes, beef, applesauce with tapioca or sago, and thin, well dextrinized toast. A little later foods which cause trouble may be tried out, one at a time. These foods are such as milk, chocolate, egg, and coffee

The patient who has had only the few foods mentioned above for a trial of 2

days may continue to show symptoms. If he does, it may be that his trouble is not to food sensitiveness, or that he is sensitive to one or more of the few foods served to him. He is now placed on a second elimination diet, consisting of beef, asparagus, string beans and gelatin. This is given 2 days trial. If this does not help, possibly the patient is not food sensitive. A further trial may be given by restricting the patient to maple sugar and water for 48 hours.

Dr. Alvarez stresses the fact that these elimination diets are only for diagnosis. The patient should not remain on them as is often the case. If a patient happens to be allergic to some very common food, it is often necessary to search the "food markets of the world," as he says, to find substitutes Rice, barley, rye, oats, millet, lima beans, sago, and tapioca may be substituted for wheat. The soy bean is being used a great deal in the United States at present and is valuable for its high protein content.

Oils derived from sesame and rape may be used by those who are allergic to our common ones. The avacado or alligator pear can supply much fat to those who cannot take other fats.

FOOD ALLERGY AND SENSITIVENESS

The influence of diet on cutaneous disease, says G S Williamson, is necessary to emphasize the relation of the skin to internal organs. Diseases in any 1 part of the body can be reflected in distant and apparently unrelated structures. The skin is no exception to this important rule. The influence of nutrition on the skin is an important factor and in order that there is a proper performance of its function, it is necessary to give an adequate diet.

"There are numerous dermatological diseases of serious nature, and which nutritional errors are not causative, diet has an important place in their management. A few such diseases are: Pemphigus; dermatitis exfoliative, leukemias, Hodgkin's disease, acute disseminated lupus erythematosus, and new growths."

The following are a few diseases or disease groups in which the factor of diet is specifically concerned.

- 1 Vitamin Deficiencies—The rôle of vitamins is of considerable importance, but it is discussed in detail in another chapter of this book.
- 2 **Tuberculosis** In the last few years the dietetic treatment of cutaneous tuberculosis has been greatly stressed.

Sauerbruch, Herrmansdorfer and Gerson advocate a diet that virtually excludes sodium chloride. For short, this is known as the S H G salt-free diet Following are the essentials of this diet:

(1) Sodium chloride is almost completely excluded, but the diet is rich in calcium and other minerals, (2) a large amount of uncooked vegetables (cooked vegetables should be prepared in waterless cookers in their own juices); (3) meats are restricted; (4) raw eggs, milk, butter and meat juices are included, (5) large quantities of vitamin C and D are included, (6) a diet high in fat and protein but low in carbohydrate

The sodium ion of common salt appears to be the component which retards healing in skin tuberculosis

3 Acne Rosacea—"Acne rosacea is a disturbance of the small blood vessels (capillariea) of the central, or flush, area of the face" Digestive disturbances are one of the outstanding features of this disease and are important etiologically. The symptoms may be brought on by errors in the diet, especially from the excessive use of tea, coffee, alcohol and condiments. Many of the patients have

some degree of hypochlorhydria. Diet is one of the most important features of the treatment. In mild cases the proper diet is sufficient to effect a marked improvement, and sometimes a cure. The dietary principles involved are as follows: (1) All stimulating foods, such as tea, coffee, alcohol, condiments, excess sweets and rich gravies are excluded; (2) a bland diet of small frequent feedings is preferable; (3) excessively hot foods should be avoided; (4) the administration of dilute hydrochloric acid when necessary; (5) the correction of gastro-intestinal disturbances.

- 4. Yeast Infections (Moniahasis)—
 "A wide variety of skin lesions are caused by yeast or thrush microorganisms, and closely resemble ringworm infections. Probably the commonest example is oral thrush in infants." Yeast infections are occasionally present in diabetics and in obese patients and are, therefore, of dietetic interest. The carbohydrate intake should be limited and in every instance diabetes should be suspected.
- 5 Disorders of Metabolism-A primary cause of any specific skin lesion is known to be caused by an alteration ın carbohydrate metabolisin There is a series of skin affections which result from disorders of fat metabolism. The following 2 are of dietetic importance: (1) A group of lesions known as xanthomas which may be found on the skin or involving internal structures There is 1 form known as xanthoma diabeticorum, which is associated with diabetes. The diet is directed largely toward controlling the diabetes and is fat poor in order to lower the cholesterol and fat content of the blood. (2) Necrobeosis lipoidica diabeticorum is a rare disease, the result of disturbed fat metabolism in which the excess fat present in the blood of diabetic patients is deposited in the skin The treatment is the administration

of *insulin*, *limitation of fat*, and a diet suitable to control the hyperglycemia.

The cutaneous manifestations of food allergy are wide in variation and severity. They principally consist of: Urticaria (hives); angioneurotic edema (giant hives), eczema (atopic dermitis), petichial eruptions (purpura), acne vulgaris, and, not infrequently, various degrees of itching.

- 1. Urticaria and Angioneurotic Edema—These show variations of the same fundamental disturbances. They are fairly common results of food allergy. The foods that are the chief offenders in infants are eggs and milk; in adults, eggs. meat (especially pork), fish, shellfish, nuts, tomatoes, and particularly wheat cereal. Alcoholic beverages are not uncommon causes of urticaria.
- 2. Pruritus (Itching)—This condition, with no evidence of skin lesions, is a frequent offender. Elimination diets are of value in this disease.
- 3 Purpura—This can be caused by food allergy The following foods are known causes of purpura eruptions Eggs, milk, wheat, chocolate, beef, pork, certain fish, onions, tomatoes, and strawberries
- 4 Acne Vulgaris This affects the voung adult most often. The present opinion is that the type of diet is not at fault, but rather a sensitivity to certain specific foods. Although a hypersensitiveness may develop, the foods that are commonest offenders are chocolate, fish, nuts, white bread, and the salts of bromide and iodine.
- 5. Atopic Dermitis This is the cutaneous lesion in which food allergy assumes a rôle of great importance. The foods that are the greatest offenders are eggs, wheat, and milk, although no foods are beyond suspicion.

In the treatment of skin lesions resulting from food allergy, the first and most

essential step is a detailed and careful history; the second, skin tests by the scratch method. The treatment of the patient showing positive skin reactions to foods should be first, the avoidance of these foods; second, the use of elimination diets when offending foods can not be determined; third, desensitization when such procedure is indicated.

GASTRIC ULCER

The diet for bleeding gastric ulcer which has been used by Andresen in the Long Island College Hospital from 1925 to 1936 has proved so very successful that John S. LaDue, M.D.,6 reports on it in detail. The purpose of the diet is to stop bleeding by formation of clots, to keep the blood pressure down, manage shocks, and prevent digestion, by gastric secretion, of the exposed wound in the blood vessel.

The patient must rest, be kept warm No ice is permitted.

Following is a copy of the treatment.

TABLE III

LONG ISLAND COLLEGE HOSPITAL DIET FOR PATIENTS WITH GASTRIC HEMORRHAGE

	Ounces
(HARACTER OF FFFDINGS	
GELATIN SOLUTION-	
Gelatin	1
Lactose	3
luice of 1 orange	
Water	32
GRUEL MINTURE No 1-	
Cereal gruel (oatmeal, barley o	r
cornmeal)	. 16
Mılk	14
Cream	4
Lactose	3
GRUEL MIXTURE No 2-	
Cereal gruel (same)	12
Milk	32
Cream	4
Lactose	4

TABLE III (Continued)

Schedule of Feedings
First and second day; feed every 1½ hours—
Gelatin solution 4
Third day; feed every 1½ hours— Gelatin solution 4 Gruel No. 1
Fourth day, feed every 1½ hours— Gelatin solution
Fifth and sixth day: feed every 1½ hours— Gelatin solution 6 Gruel No. 2* 6
Seventh and eighth day, feed every 2 hours— Gelatin solution 6 Gruel No 2* 6
Ninth day and thereafter—Long Island College diet for patients with ulcer
TABLE IV
Long Island College Hospital Diet for Patients with Ulcer
Breakfast—Milk, 8 oz, with cream if desired, cereal, 5 oz, with milk or cream; egg, 1, soft boiled or poached, fruit juice or stewed fruit (end of meal)
MIDMORNING MFAL—Milk, 8 oz, cream, ½ oz, lactose, ½ ounce, with cocoa if desired, always with crackers, toast, bread or cake LUNCHION—Milk, 8 oz baked or mashed
potato or plain spaghetti, egg, 1, soft boiled or poached, or cream cheese, bread and butter, 2 slices, pudding, custard, gelatin,

MIDAFTERNOON MEAL-Same as midmorning

BEDTIME MEAL-Same as midmorning meal;

MEDICATION—Olive oil, 1/2 oz. 3 times a day

repeat every 21/2 hours during night if awake.

before meals; liquid petrolatum, ½ oz, every

SUPPER—Same as breakfast or luncheon

ice cream, or stowed fruit

night, water, if desired

meal

GASTROINTESTINAL DISEASES

A. H. Douthwaite⁷ discusses gastritis and the dietary treatment. The diet should be free from alcohol, iced drinks, and ices, spiced food, very hot food or drink, salted foods, mustard, sauces, shell fish, smoked meat or fish, pastry, new bread, food containing pips, skins, nuts, strong cheese, coffee, and strong tea and salads (except in strict moderation). Food must be thoroughly chewed.

The type of diet which he suggests for peptic ulcer is shown below. He believes that drugs are of little importance in the control of acidity, and that frequent feeding is most important. The more liberal diet is approved.

Gastric and Duodenal Ulcer

Treatment—(1) Rest in bed until 2 consecutive negative reports for occult blood in the stools have been obtained.

(2) Diet-Frequent feedings are important in order to neutralize gastric acidity and to diminish spasm. For the first 2 weeks, they should be given at 9 A M , 11 A M , 1 P. M , 4 P. M., 7 P. M., and 10 P M, but if the patient should wake in the night he should take a further feeding of milk or biscuit. The types of foods permissible are milk, cornflour, Benger's (of these 2 pints in 24 hours), force, cornflakes, 4 slices thin bread (no crust), and butter and honey (at the 1 P M feeding), cream, 1 lightly boiled or poached egg, weak tea, sugar, custard, junket, strained fruit juice, strained tomato juice After the end of the second week if no pain is now felt, the milky foods may be reduced and fish, fat bacon, rusks, 2 more eggs, sieved and carefully prepared purée of vegetables and fruits added. The solid foods must be thoroughly chewed. In the fourth and subsequent weeks, the breast of bird may be taken if thoroughly chewed

^{*}Add to gruel mixture at each feeding one of the following 3 oz. cereal, 1 soft cooked egg, custard or jello.

From now on for the rest of the patient's life he should avoid meat soups, meat extracts, spiced food, effervescing drinks, all spirits, all alcohol on an empty stomach, the fiber of fruit and vegetables, this, therefore, includes salads, raisins or food containing pips, skins, and nuts. Butchers' meat may be taken after the end of two months of treatment.

Milk at 11 A. M., bedtime, and in the night is important.

(3) General Measures important at All Times—

- (a) Masticate food well.
- (b) Never hurry over a meal—rest if only for ¼ hour afterward.
- (c) The first sign of indigestion is an indication for rest in bed and medical advice.
- (d) Do not go without regular and frequent meals.
 - (e) Avoid exposure to cold.
 - (f) Have regular dental attention.

(4) Medicinal:

- (a) Olive Oil—Two teaspoonfuls before the main meals if not nauseating.
- (b) Hyoscyamus—The tincture in doses of 10 to 15 minims (0 6 to 1 cc) to diminish spasms—give 4-hourly between meals, for 6 months or more
 - (c) Alkalis.
 - (d) Liquid paraffin for constipation
- (c) Phenobarbital—One-half grain t i d. (0.03 Gm) for the nervous patient for the first 6 weeks

The commonest cause of relapse is mental stress and worry. Smoking is worse than alcohol for ulcers Both are bad, especially on an empty stomach. The safest alcoholic drinks are light beer or well diluted gin with lime juice and water (1 "finger" of gin to a tumbler).

Peptic Ulcer

A definition, as given by A. H. Aaron⁸ for the cause of peptic ulcer is: "For some unknown reason the mucosa of the stomach and duodenum loses its ability to resist the digestive action of hydro-

chloric acid and pepsin." Therefore there is evidence that the control of the acidity is the basis for the treatment of peptic ulcer of the stomach and duodenum The best treatment has been a bland diet. proper feeding times, and alkali therapy. The bland diet does not include condiments which stimulate the flow of hydrochloric acid, and roughage which irritates and prevents healing; it includes those foods which diminish acidity, such as fats, butter, cream, and proteins which utilize more hydrochloric acid than other foods, and frequent feedings so that the stomach is not allowed to accumulate acid secretion of high concentration. It must be realized that gastric secretion occurs during sleeping hours and therefore it is necessary to wake the patient and give him a glass of milk, or a slice of bread and butter. If there are adequate amounts of fruit juices, milk, meat, eggs, and soft green vegetables included in the diet, there need be no fear of the patient developing a vitamin deficiency.

BLAND DIET

FRUIT JUICES-

May have cherry, loganberry, orange, pineapple, and strawberry Orange juice, 2 to 4 tablespoons daily. These must be taken after any meal.

Avoid all other fruit juices.

Soups-

May have soups made with sweet cream or milk and the following strained vegetables—peas, celery, asparagus, potato, mushrooms, and oyster stew

Avoid clam broth, meat broths, and boullions MEAT, FISH, or FOWL—

May have beef, chicken, turkey, lamb, veal, sweetbreads, liver, bacon. Any freshwater fish. Prepared—broiled, boiled or baked Avoid highly seasoned meats, sausages, etc, fried or fat meats, fish, or fow!

VEGETABLES-

May have cooked—beets, asparagus, broccoli, lima beans, carrots, wax beans, squash, finely chopped lettuce, peas, white and sweet potatoes, cauliflower, spinach Baked, pureed, mashed or boiled

Avoid all other vegetables, either raw or cooked.

Breads-

May have toast, day-old white bread, fine rye bread, soft rolls, soda crackers, zweibach.

Avoid fresh bread, hot breads, bran or whole wheat breads.

Eggs-

May have soft boiled, poached, scrambled, hard boiled, coddled, or omelet.

Avoid fried.

FATS-

May have butter, cream, olive oil, oleomargarine, and crisco

Avoid all fried foods

CEREALS-

May have cream of wheat, wheatena, farina, hominy, tapioca, strained oatmeal, ralstons, rice, macaroni, spaghetti.

Avoid all coarse grained cereals and bran

Nuts-

None allowed

CHEESE-

May have cream, cottage, brie, and mild American types

Avoid all others

GRAVIES, SAUCES, AND CONDIMENTS-

May have mayonnaise or boiled dressing, plain flour gravy with small amount of meat seasoning

Avoid all sauces and condiments Pepper and salt not allowed except as used for moderate seasoning in preparing food

FRUITS-

May have applesauce, baked apple without skins, stewed apricots, peaches, prunes, pears

Avoid all other fruits—raw and cooked

DESSERTS-

May have gelatin, custard, prune whip, rice, tapioca, and other simple puddings, vanilla ice cream or sherbets, charlotte russe, angel food cake or sponge cakes with white frosting, plain chocolate candy

Avoid chewing gum, pies, pastries, and all other cakes and cookies

BEVERAGES-

May have cocoa, eggnog, malted milk, milk, cream, weak tea, Postum, Kaffee Hag, water, chocolate milk shake

Avoid coffee, tea, alcoholic drinks, very hot or very cold drinks

Between meals and at bedtime take a glass of milk or a slice of bread and butter

GOUT

E. C. Bartels⁹ tells us that there have been many experiments done on patients suffering from gout. Diets high in fat and low in carbohydrate have been used, purine free diets, high protein and carbohydrate and low fat diets have been administered. The author has tried a low purine, low fat and high carbohydrate diet with the administration of cinchophen with desired results, that of preventing further attacks of joint pain. The general directions for the diet are shown in Table 5.

TABLE V

FOODS FORBIDDEN-

Kidney, liver, sweetbreads, sardines, anchovies, brains

Alcoholic beverages

Whole-grain products, such as whole wheat bread, shredded wheat, oatmeal.

Asparagus, beans, cauliflower, peas, lentils, spinach, mushrooms.

Condiments, gravy, meat soups, meat extracts.

Butter, cream, mayonnaise, fat-containing foods

FOODS PERMITTED-

Milk (skimmed)

Eggs

Fruits

Vegetables, except as listed above

Cereals, except whole grain

Cottage cheese.

Breads, except whole wheat

Jelly, gelatin.

Potatoes, rice, macaroni, spaghetti, noodles Cocoa, coffee, Postum or tea—1 cup daily MEAT, FISH, FOWL (amount permitted depends on severity and progress of case)

Beef (lean)

Veal.

Chicken.

Herring

Oysters

Crab

Cod

Whitefish

Bluefish

Finnan haddie

Tuna.

SAMPLE MENU

BREAKFAST Fruit Average serving Cereal Average serving Egg 1 Milk (skimmed) 1 glassful Toast 2 slices Jelly or honey 2 tablespoons Sugar as desired DINNER AND SUPPER Vegetable soup made without meat Lean meat Small serving (as or permitted) Egg Potato, rice, macaroni, spaghetti, noodles 1 serving Vegetables ⅓ cup Salad, if desired Bread 1 slice Jelly or honey 2 tablespoons Milk (skimmed) 1 glassful

Fruit

The amount of meat, fish, or fowl to be taken depends on the severity of the disease. These foods contain some purine but should be included to satisfy the patient. At the beginning of the treatment, the meat, fish, and fowl are restricted to 1 serving 2 or 3 days a week and are increased until they are taken daily if the uric acid level permits. The sample menu contains approximately 278 Gm carbohydrate, 77 Gm protein, 22 Gm. fat, 1618 Calories. The carbohydrate is increased so that the Caloric intake may be made adequate for the patient.

Average serving

INFANT FEEDING

Charles H. Smith¹⁰ states that it is both undesirable and dangerous to feed an infant more food than he needs.

It is known that the mother's milk "does not come in" until the third or fifth day. It has been demonstrated by C. H. Smith that the baby gets about 1 or 2 ounces of breast milk a day in the first few days, 6 to 10 ounces by the end of the week and 10 to 15 ounces at the end of the second week. It has been proved that the most that the babies get is between 25 and 30 Calories per pound in the first week, 30 to 45 Calories in the second week From the second week on the average is about 45 Calories per pound. The baby begins to gain as soon as he receives 30 Calories per pound but he will stop gaining in the third week if he does not receive 45 Calories per pound.

"For more than a generation a plan for bottle feeding which closely imitates the Caloric intake of the breast-fed infant has been used with success. This starts with $\frac{1}{4}$ strength milk (5 ounces in 20 or 21 ounces total) plus $\frac{1}{2}$ to $\frac{3}{4}$ ounces sugar. It is increased every other day to $\frac{1}{3}$ milk at 1 week and $\frac{1}{2}$ milk at 2 weeks."

The routine on the Children's Medical Service of Bellevue Hospital is as follows:

Dav	1	2	3	4	5	6	7	8	9	10	11	1.2	13 14
Milk, ounces Water, ounces Cane sugar, ounces	0 10 1⁄2	5 16 1/2		6 15		7 14 23		8 13		9 12	ř	10	11 10
Energy quotient at 7 lbs		23		26		30		35		38		+1	1 44

diet is inadequate in vitamin A and B, and therefore concentrates must be given. The patient frequently loses weight until he learns to consume enough carbohydrate to make up the Calories lost by cutting down the fat.

Six feedings of 3¹2 ounces, or 7 feedings of 3 ounces. (The smaller babies will not even take all of this in the first days.) When using this routine, the weight curves are exactly the same as those of breast-fed infants

The second step of feeding infants is between the third week and the time when other foods are added. The time to start adding the other foods is usually at about 6 months.

The average Caloric intake at 1 year is usually about 45 Calories per pound or 100 calories per kilogram. The minimum protein requirement is equal to the amount contained in 11/2 ounces of milk per pound body weight. Some advantage is gained by giving a little more (about 13/4 ounces per pound), but a baby rarely needs as much as 2 ounces per pound. By giving 1¾ ounces milk per pound, it should yield about 35 Calories per pound so that only 10 Calories of sugar (about 1/12 ounce per pound) would be needed. Usually, by the time the baby reaches 12 pounds, an ounce of sugar is needed, the physician starts to add cereal so that the sugar need is not increased over this amount Smith feels that it is much more accurate and scientific to weigh the added sugars; and this can be done easily on any small postage scale

The fluids required in the early months are about 3 ounces per pound and in the later months about 2 ounces per pound. All the water may be given in the bottle or a part held from the milk dilution and given separately

Supplement foods to the bottle may be started at almost any time. But there is no particular advantage in starting them very early. The following table gives a reasonable time for each:

The feeding may be reduced from o to 7 feedings to 4 feedings toward the end of the year. The time may be spaced in 2 ways at either 6 A. M., 10 A. M., 2 P. M., 6 P. M. or 7 A. M., 12 M, 5 P M., 10 P. M. The latter plan has many more advantages than the former. When the baby is fed at 10 P. M., he is less likely to awaken early and during the winter it is easier to get him out of doors from 10 A. M. to 12 M. and 2 P M. to 4 P. M

Occasionally, at the end of the first year, babies will do well on 3 meals a day, with orange juice and a cracker in the afternoon. Some babies will go on the 3 meals a day at 9 or 10 months and others not until after a year. It is not wise to force a small baby, or 1 whose appetite is not very good to take the food needed in 3 feedings because it is then difficult to get in enough milk. It is not advisable to give milk between meals as the appetite and digestion are apt to be upset, since milk needs nearly 4 hours to digest

The list on page 115 gives an adequate diet for a child of 1 year weighing 22 to 23 pounds. All tablespoons should be level

This diet yields approximately 1000 Calories, which is adequate for a 22-pound child Cevitamic acid is necessary. It is given in either the form of fruit juice or tablet form a few weeks after weaning. It is not necessary during breast feeding. The best available source of vitamin D is sunlight given on the skin or, if this is

Foods	Time	Amount at Beginning	Amount at One Year
Cereals	4- 5 months	1 level tablespoon	3-4 level tablespoons (twice a day)
Vegetables	5- 6 months	1 level tablespoon	2-3 level tablespoons (twice a day)
Potato Meat juice Scraped meat Egg Cooked fruit Orange juice	6- 7 months 7- 8 months 8-10 months 9-12 months 7-12 months 2 weeks after weaning	1 level tablespoon 1 level tablespoon 1 teaspoon 1 yolk 1 teaspoon 1 teaspoon	1 small potato 4 tablespoons 1-2 tablespoons 1 whole 2-3 tablespoons 1 orange

7.30-8 а.м.	Breakfast·		Note:			
	Cereal Milk	.8-12 ounces	No egg is needed for breakfast			
12 00 м.	Lunch:					
	Meat or egg Potato, rice or macaroni Vegetables Junket or custard	2 tablespoons	No added milk to drink			
400 р.м.	Orange juice and cracke	er	No milk in midafternoon			
5 30-6 р.м						
	Cereal Mılk Cooked fruit	4 tablespoons 8 to 12 ounces 2 to 4 tablespoons				
10 00 р.м	Mılk	4 to 6 ounces may l 8 ounces are take	to 6 ounces may be given if wanted and if only 8 ounces are taken at breakfast and supper			

not available, as on cold or cloudy days, it may be given in any one of the dozen forms on the market. All other vitamins are present in ample amounts in a well balanced diet.

MINERAL REQUIREMENTS

John H Talbott and Frederick S. Coombs¹¹ review the observations of Loeb, who observed that a patient with Addison's disease suffered from an insufficiency of sodium chloride in the body. It has now been confirmed that a high sodium chloride diet has increased the life expectancy of persons with this maladv A minimum of 214 drams (10 Gm) of table salt in addition to that of the diet is given as well as a diet high in carbohydrate There also appears to be a high concentration of potassium in the serum, so Wilder has recommended a low potassium intake No meat, fish, fowl, dried vegetables, or fruits and nuts should be used, or they should be restricted to very small amounts

They suggest a high sodium intake in any acute fever. Foods such as broths, soups, and other salty fluids may be used with an addition of 1½ to 2 drams (6 to 8 Gm.) of table salt. Persons who do very strenuous work, especially in warm weather require at least 3¾ drams (15 Gm.) of sodium chloride daily. Diabetes insipidus is 1 condition which at present, as far as is known, reacts unfavorably to an increase in salt. Extreme thirst is experienced If the diet contains less than 1¼ drams (5 Gm.) of salt, the patient has a feeling of "well being."

OBESITY

Horace Gray and Dorothy E. Kallenbach¹² report on the results of obesity treatment of 212 obese outpatients from June, 1933, to March, 1938. Many were sifted out of the group as time went on, which resulted in a very co-operative group remaining. There were 106 who remained throughout The diet used was as follows:

- 1. Protein, 06 to 10 Gm per kilogram of body weight in adults; 20 to 30 in children
- 2. Calories, 10 per kilogram at the start, and reduced, let us say, once a week by decreasing the carbohydrate and fat until weight is lost.
- 3. A common diet accordingly would be about C 80, P. 60, and F 40, yielding 900 Calories and a FA/G ratio of 05 for a patient

weighing 200 lb. (90 kg.) this would be about 10 Calories per kilogram.

- 4. The satiety value is perhaps the next thing to consider; that is, keeping the patient sufficiently satisfied so that the diet will be adhered to. This is largely achieved by increasing the bulk by means of 5 and 10 per cent vegetables.
- 5. Vitamins and minerals are considered by taking care to include the following in the diet. Vegetables (A and B); fruits (C); about 30 Gm. cheese or more if the patient will take it, or milk about ½ pint—240 cc. (for calcium and phosphorous); and cod liver oil, 1 teaspoon—4 cc.—a day (A and D).
- 6. Fluids are discouraged at mealtime in order to reduce the common tendency of bolting food
- 7. Amount of weight lost each month is preferred to be 4 to 8 pounds (17 to 36 kg.) rather than larger amounts which predispose to wrinkles, irritability, and perhaps more serious upsets
 - 8 Bread is generally discouraged.

The authors believe in "no tapering off," but an abrupt renunciation They believe in a flour-free diet and tell the patient that they must go without all flour for 30 days. This, they are told, means no bread, white, wholewheat, brown, yellow, or toasted—no melba toast—no rye wafers—no crackers—no pastry—no pancakes.

Patients were made to bring in written lists of what they had eaten the day before coming in to see the doctor Their average weight was 202 pounds (91.8 kg). Some patients were able to reduce on the diet alone. Others did receive drugs. They believe that frequent checkups must be made. The interval should not exceed 3 months.

PREGNANCY

Maurice B. Strauss¹³ gives the following table to show an optimal diet in pregnancy:

TABLE VI

An Optimal Diet in Pregnancy Includes Daily:

Fruit	200	Gm
Eggs (3)	180	Gm
Milk	1000	cc
Meat, fish or		

poultry 300 Gm Vegetables 400 Gm.

Butter, sugar, cereals, breadstuffs, etc, to be added to furnish sufficient calories.

At least 3 grains (0.2 Gm.) of ferrous sulfate and 800 U S. P. units of vitamin D should be given in addition

This is a splendid diet but Dr. Strauss fears that it is too expensive and beyond the reach of the average patient who attends the clinic. However, he feels that a person may get along well on less but will not experience the feeling of optimal nutrition. Possible results of vitamin deficiencies are many. There is no evidence at present to prove that urinary infections, such as pyelitis and pyelone-phritis in pregnancy may be due to lack of vitamin A, yet Dr. Strauss believes that it is wise to eliminate the possibility and use plenty of foods rich in vitamin A.

A deficiency of vitamin B₁ or B₂ may lead to the "toxic" polyneuritis of pregnancy and cardiovascular abnormalities. as well as pernicious anemia of pregnancy. It should also be remembered that patients who do not receive adequate amounts of vitamin C bleed very easily and show very poor wound healing. The demands made upon the mother for calcium can only be supplied by the use of 1 quart of milk daily. This need not be grade A The fat content is not important and skimmed milk is just as satisfactory. It may also be better to use skimmed milk to keep down the calories, if the pregnant woman has a tendency to gain too much weight. If vitamin D is absent, then calcium is not absorbed from the gastrointestinal tract The mother

should get at least 800 units of vitamin D; therefore, cod-liver oil should be given in some form. It has also been thought that hemorrhagic disease in infants may be due to a lack of maternal vitamin K.

If protein intake is not adequate, the labrile reserve of protein is used first and then the less readily dispensable reserve protein and the plasma protein. When the plasma protein begins to go, the balance between the intracapillary hydrostatic pressure and the colloid osmotic pressure of the blood becomes disturbed. Extra cellular tissue fluids result from water filtering out of the capillaries faster than it returns.

Fifteen or more pounds of water may accumulate before it will be noticed as edema. Many women think they are merely gaining weight.

Since the average or even the optimal diet contains but little iron, it may be necessary to take iron in its medicinal form Deficiencies really would be commoner, but for the fact that the body is most economical. It uses the iron from the wornout red blood cells A mother should be prepared for loss of blood which would deplete her iron reserve.

Strauss says in conclusion that "many of the toxic manifestations of pregnancy, polyneuritis, simple anemia, pernicious anemia, preeclampsia, and certain cases of eclampsia among them, appear to result not from the action of mysterious and undiscovered 'toxins' but from inadequate maternal nutrition and that this may manifest itself not only in ill health of expectant mothers but also in disorders in their infants."

RENAL DISEASES

T. P. Sprunt¹⁴ states that the chief questions to be settled in relation to diet

of the patient with renal disease are how much water, how much protein and how much salt should be given or to what extent these things should be withheld. Because of the newer knowledge of nutrition and metabolism many clinicians are now convinced that routinely restricted diets based only upon the fact that the patient has a renal disease are not justified. The fact has been recognized that restricted protein may sometimes result in protein starvation and the restriction of water and salt may be harmful as well as adding materially to the patients' discomfort. The tendency at present is to give them an adequate diet except in a few and brief emergencies.

It has been shown by observation and dietary experiments that a man may live in apparent health on as little as 40 Gm. protein per day, or he may eat as much as 280 Gm. a day. The total energy provided by proteins in these diets therefore varies from about 8 per cent to about 44 per cent, but the general range among the white race is from 12 per cent to 16 per cent. The optimum protein requirement varies under different conditions. but it is generally believed to be from 1 to 1½ Gm. per kg. of body weight. The proteins of food differ in their biological value, depending upon the aminoacid content. Human proteins are more easily manufactured from those contained in milk, cheese, meat, fish, and eggs than from the proteins derived from vegetable sources.

It has been pointed out by McCann that the catabolism of protein in the nephritic patient is influenced by the same factors that operate in most other individuals. There are the possibilities of limiting protein catabolism by means of a high caloric diet, the emphasis being placed upon the intake of carbohydrate as a protein sparer. A factor of impor-

SAMPLE DIET

For a patient with glomerular nephritis (chronic, active stage): Prescription—Alkaline ash diet of 2500 Calories Protein 70 Gm.; high carbohydrate; salt-poor; fluids limited to 1200 cc.

Foods	Amount	Grams		Ash, cc.		
Foods	Amount	Protein	Fat	Carbohydrate	Acid	Base
Fruit (orange juice) Cereal (oatmeal) Sugar .	200 cc 34 cup 1 T	1 4		20 23 15	4.0	10 0
Milk . Toast Butter	½ cup 2 slices 1 sq.	6	5 0 6 5	6 32	20	2 8
Jelly . Coffee Sugar Cream	2 T. 120 cc. 2 t 2 T.	1	6.0	10		
Cream		16	17.5	137	60	12 8
Meat Vegetable (5%) Potato Bread Butter Fruit Sugar	3 oz 5 oz 5 oz. 1 slice 2 sq 1 ser. 1 T	21 1 3 3 1	9 0	5 27 16 30 15	14 0	9 0 10 7 5 0
		29	22 0	93	15 0	24 7
Egg Potato Vegetable Bread Butter Jelly	1 7 oz 5 oz 2 slices 3 sq 1 T	6 4 1 6	60	40 5 32 15	5 5 2 0	14 0 9 0
Milk dessert Milk	1 ser 8 oz	3 8	4 0 10 0	30 12		2 8 5 6
		28	39 5	134	7.5	31 4
		73	79 0	364	28.5	68 5

Excess base 40.4 Calories 2459 Diet contains 680 cc. fluid. Amount allowed 1200 cc Amount water 520 cc.

If higher protein is desired, more milk can be added to above diet and the amount of water decreased. This would also increase excess base.

If more base is desired, fruit juice may replace the amount of water allowed

tance in the protein metabolism of certain nephritics is the decided loss of protein through the glomerular membrane into the urine and therefore there is a reduction of the blood plasma proteins

There have been many controversies as to whether a high protein diet damages the kidney, but the weight of the evidence is strongly in favor of the conclusion that neither the healthy nor the diseased kidney is damaged by a protein intake considerably higher than that to which the normal American is accustomed.

One of the results of marked nephritis and uremia is acidosis. Because of the threat of acidosis in most cases of renal disease it is customary to take care that the total diet should on combustion leave an alkaline ash. One should remember in this connection that meat, cereals, and

SAMPLE DIET

For patient with nephrosis: Prescription—2500 Calories; Protein 100 Gm.; high carbohydrate; low fat; salt-poor; fluids limited to 1000 cc.

Foods	Amount	Grams				
2 9040	Imount	Protein	Fat	Carbohydrate		
Fruit . Cooked fruit Sugar	1 orange 5 prunes 1 t.	1 1		10 35 5		
Cereal Sugar	3/4 cup 1 T.	3	The second secon	24 15		
Skimmed milk for cereal Bread	120 cc. 1 slice	4 3	1	6 16		
Butter Eggs	1 t. 2	12	12 12			
		24	17	111		
Meat Potato Vegetable Bread Butter Jelly Milk dessert Milk, skimmed or buttermilk	3 oz. 5 oz 3 oz 2 slices 1 t 2 T 1 ser. 240 cc.	21 3 1 6	9 4 4 2	30 3 32 30 30 12		
		42	19	137		
Meat Potato Vegetable Bread Butter Fruit, canned or cooked Angel cake—cake without fat	3 oz. 5 oz. 3 oz. 2 slices 1 t 1 ser 3½ in arc	21 3 1 6	9	30 3 32 30 49		
		37	13	144		
		103	49	392		

Calories 2421.

Fluid in diet 360 cc. Amount allowed 1000 cc Amount as water 640 cc

eggs yield an acid ash, milk, green vegetables and fruit yield an alkaline ash; and butter, other fats, sugar, cornstarch and tapioca produce a neutral ash

At the beginning of an acute glomerular nephritis or in uremia with chronic nephritis the physician usually orders the *Karell diet* (800 cc milk daily divided into 4 feedings), changing after several days to a Karell diet with carbohydrate supplement (the addition of fruit juices with added glucose), and on further improvement a cardiac soft diet, salt-free or salt-poor.

- T P. Sprunt states that as soon as it is possible the physician should order the full sustaining diet, keeping in mind the following points of importance:
- 1. The patient's general nutrition. Bright's disease is usually a wasting disease and the patient undernourished, but sometimes the patient may be overweight. If the patient is overweight the caloric intake may be adjusted so that there is a gradual loss of weight. But more often one wishes to improve the general state of nutrition including the store of body fat

SAMPLE DIET

For patient with chronic nephritis without edema. Prescription—Alkaline ash diet of 2500 Calories; Protein 70 Gm.; salt and fluid as desired

Foods	Amount		Gran	Ash, cc		
r oods	Amount	Protein	Fat	Carbohydrate	Acıd	Base
Fruit (orange juice) Cereal .	200 cc. 34 cup	1 4		20 23 15	4.0	10.0
Sugar Milk . Toast	1 T 240 cc. 2 slices	8 6	100	13 12 32	2 0	5 6
Butter. Jelly Coffee .	1 sq. 2 T as desired		6.5	30		
Sugar Cream	2 t 2 T	1	60	10		
		20	22 5	143	60	15.6
Meat Vegetable Potato. Bread. Butter	2 oz. 5 oz. 5 oz. 1 slice	14 1 3 3	60	5 27 16	10.0	9 0 10 7
Fruit Sugar Milk	2 sq. 1 ser. 1 T. 240 cc	1 8	13 0 10 0	30 15 12		5 0 5 6
	1	30	29 0	105	11.0	30 3
Egg Potato—large Vegetable Bread Milk dessert Milk Butter	1 7 oz. 5 oz 1 slice 1 ser 240 cc 3 sq	6 4 1 3 3 8	4.0 10 0 19 5	40 5 16 30 12	5 5	14.0 9 0 2 8 5 6
		25	39 5	103	6.5	31 4
		75	82 0	381	23 5	77 3

Excess base 538 Calories 2562

Certain types of food are usually forbidden to patients with renal disease. Some of the foods forbidden are: Salted meats, salted fish, pork, sausage, bologna, meat broth, gravies, alcohol in any form, the internal organs of animals, "in view of experimental work indicating the nephrotoxic action of products of nuclear material" Particularly in patients with cardiac weakness, the so-called "gas forming" vegetables as cabbage, cucumbers, lima beans, navy beans, turnips, radishes, should be avoided, although patients who have no symptoms of gaseous indigestion may eat them.

- 2. There should be adequate protein in the diet and at least 50 per cent should be of animal origin and therefore of high biological value. The usual amount of protein ordered in an average case is 70 to 80 Gm. If there is a marked retention of nonprotein nitrogen, the protein of the diet should be lowered to 50 Gm with a larger percentage of it being of animal origin.
- 3 A high Caloric diet that is made up largely of carbohydrates is often needed because of the patient's poor nutrition and also because with a moderate protein intake and a higher carbohydrate diet

the protein catabolism is reduced to a minimum and 1 of the important dietary indications in nephritis is met.

4. The diet should be prepared so that the alkaline, acid and neutral ash foods are in such proportion as to yield a basic ash in excess. The excess base should amount to from 25 to 50 cc. in 24 hours and each meal should contain at least 5 cc. excess base. The following tables give the value for 100 Gm. food in terms of cc. of N/10 acid or alkaline needed to produce neutrality.

FOOD PRODUCING AN ALKALINE ASH

Vegetables (except corn and brussels sprouts) Fruits (except prunes, plums, and cranberries) Cow's milk Potato Almonds	cc N 10 alkaline per 100 Gm. 6 0 5 0 2.3 7.0 12 0
1 IIII Olida	120

FOODS PRODUCING AN ACID ASH

		cc N,'10 acid per 100 Gm.
Meat		14
Eggs		11
Bread		3
Cereal		12
Peanuts		4
Oysters		30

5. The fluid and salt intake must be regulated by the presence or absence of edema." It is customary to restrict salt in almost all types of nephritis and the restriction is helpful in the cases with edema or with threatened edema but actually harmful in cases of chronic nephritis without edema that show very marked polyuria with fixed low specific gravity of the urine." One objection to the absence or marked restriction of salt in the diet is the bad effect on the patient's appetite and the inability for him

to consume a nutritious diet. For the most part physicians use salt-free diets (no salt used in cooking or preparation or at the table) for only a few days at a time. A salt-poor diet is preferable; in this a moderate amount of salt is used in cooking, including the use of salt in bread and in butter but no extra salt added at the table and that furnishes from 3 to 5 Gm. a day.

Where edema is present the fluid intake should be limited to approximately the same amount as the daily output of fluids. When it is necessary to greatly restrict the fluids milk can not be used in large quantities and the more succulent fruits and vegetables can not be given too freely unless the patient is willing to do without extra water.

Where there is an increased nonprotein nitrogen retention the salt intake should be kept low and the fluids increased in hopes of stimulating diuresis

Patients with marked and persistent polyuria should be permitted fluids and salt freely.

Some sample diets for disease of the kidney are on pages 118, 119, and 120

RESTRICTED DIET AND DEFICIENCIES

Dwight L Wilbur¹⁵ tells of a woman he called upon who had marked scaling of the skin of hands and face, diarrhea and nervousness. She had been placed on an elimination diet the year before for asthma. She confined her diet to only a few foods and developed the characteristic symptoms of pellagra

Wilbur points out that limited diets for therapeutic reasons may often lead to deficiency diseases. A knowledge of vitamin requirements of man, and the vitamin content of foods as well as the capacity of the patient to digest and

adequately utilize the food which he is given are all of most importance.

Reduction diets are often to blame Not the type of reduction diet given by an authority, but the self imposed type, such as coffee for breakfast, clear soup for supper and a candy bar at noon. The individual who has difficulty in digesting foods, will often limit himself to a few foods which leave him feeling comfortable He soon narrows himself down to so few that his diet is very deficient in minerals and vitamins

Following are some of the types of diets where most particular care should be given to the vitamin content of foods.

- 1 The dyspeptic who narrows himself down to tea and toast.
- 2 The food faddist, the eccentric (misinformed), the poor who cannot afford to spend much money for food
 - 3 Those on elimination diets due to allergy
 - 4 Diets for lactating and pregnant women
- 5 Diets for patients who have chronic heart and kidney disease
 - 6 Diets of growing children
- 7 Diets of patients with long standing chronic infections such as tuberculosis

The question of vitamin concentrates is settled by saying that only if it is

impossible to supply vitamins naturally in the food to more than meet the requirement, should vitamin concentrates be used. In special diet work, the vitamins most often deficient are, vitamin B complex and vitamin C.

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ENDOCRINOLOGY

By CHARLES W. DUNN, M.D.

ADRENALS

Treatment with an Adrenal Cortex Extract

The object of this report by Thompson, Thompson, Taylor and Hoffman¹ is to demonstrate the value of *adrenal* cortical extract, itself, in Addison's disease. One cc of the adrenal cortex extract used in this study represented 75 Gm. of fresh sheep adrenal.

Seven cases of marked Addison's disease, varying in age from 18 to 49 years.

all showing the typical clinical findings of pigmentation, hypotension, and the characteristic blood chemical changes, received long administration of adrenal cortex extract. Of the 7 patients, 4 are now living and 3 are dead

The 4 living patients received extract for from 1 to 3½ years. Only 1 is confined to the hospital, because of an associated active tuberculosis. The other 3 patients are able to conduct their usual activities. Untreated cases of Addison's

disease run a gradual down-hill course with spontaneous remissions and crises alternating with one another until a severe crisis causes death. The crisis is characterized by marked muscle weakness and prostration, nausea and vomiting, and occasionally, diarrhea. The hypotension and pigmentation of the skin increase and there is the characteristic increased alteration of the sodium and phosphorus values of the blood during the crisis. With the onset of a crisis, therapy must be instituted at once. This consists of the intravenous administration of 10 cc. or more per hour of an active adrenal cortex extract. The authors state that there is no danger present of giving too much extract Two intravenous administrations of 9 Gm. of sodium chloride and 50 Gm of dextrose every 6 hours are given in the form of a 5 per cent dextrose in normal salt solution. Fifty cc. of a 2½ per cent sodium citrate solution may be added to 1 liter of fluid in each 24-hour period. They substitute oral administration of sodium salts as soon as they can be retained. In the authors' opinion, large doses of extract are very important and superior to the administration of sodium salts alone Response of the patient to the adrenal cortex extract intravenously administered is striking and within 24 hours he can usually take food and sodium salt by mouth and, after 2 to 3 days of therapy, can be placed on a maintenance program Three to 4 intravenous doses of 10 cc adrenal cortical extract per hour are usually sufficient to overcome the crisis and, if the patient does not revive after 40 cc. of extract, sodium chloride should be administered intravenously at once and large doses of adrenal cortex extract continued. The onset of nausea in the case of Addison's disease should be regarded as a danger signal and the onset of vomiting gener-

ally requires administration of sodium salts.

Maintenance Treatment—After the patient has been controlled and all symptoms of the crisis have diasppeared, a maintenance dosage of adrenal cortex extract is required. Daily administration of 10 cc. or more is usually sufficient. However, the administration of about 3 drams (12 Gm.) of sodium chloride and 1 dram (4 Gm.) of sodium citrate or bicarbonate by mouth may suffice and, again, in other cases, a combination of both is required.

Diet is important and should be high in Calories and low in potassium. A favorable sign is a gain in weight of the patient and lack of weight gain should be considered as an ominous sign.

The authors believe that without large doses of adrenal cortex extract maximum improvement cannot be produced. In 3 of the fatal cases reported, their subsequent experience has shown that in all probability the dosage of adrenal cortex extract administered to these patients was inadequate

Every patient with Addison's disease requires constant observation by a physician experienced with this form of therapy, as emergencies arise, often quite suddenly Infections of all types should be avoided and, if infection does occur, should be treated as an emergency state. When the basal metabolism is low, the administration of sufficient thyroid extract to correct this state is an important part of the treatment. No aggravation of Addison's disease has been observed during the administration of thyroid extract.

Addison's Disease

Treatment with Desoxycorticosterone Esters—Ferrebee, Ragan, Atchley and Loeb² report the use of the

synthetic adrenal cortical hormone, desoxycorticosterone, in a series of 13 patients with Addison's disease. Their results are in general agreement with those reported by Thorn, et al,³ and Cleghorn, et al.⁴

Hospitalized patients usually receive 25 mg. of desoxycorticosterone acetate or propionate daily for 4 days, then from 10 to 25 mg. daily for 5 days more. The preparation used was 5 mg. of the synthetic hormone dissolved in sesame oil Both esters of desoxycorticosterone apparently have equal activity in controlling Addison's disease. Results show that the synthetic adrenal hormone brought a striking retention of salt and water. Serum sodium concentration increases to normal and is maintained at a normal level as fluid retention continues Coincident with the retention of salt and water and weight gain, which frequently varies in individual patients, is, in every case. marked decrease in urmary excretion of sodium chloride and water. The blood serum volumes increase between 0.3 and 12 liters during the first 10 days of treatment in the 6 cases in which these measurements were made. There were no constant alterations of albumin globulin ratios in the 4 cases in which this determination was made. There was a marked fall in the potassium concentration of the serum and frequently to abnormal low levels of 29 milliequivalents per liter Urinary excretion of potassium was increased on the first day of administration of adrenal cortical hormone in the 6 cases in which this factor was studied. In nonprotein nitrogen level of the serum there is a decrease, even if normal values are present at the onset of treatment There is usually a slight increase of total nitrogen excretion, however, not exceeding 2 Gm. the first 2 or 3 days of treatment. Serum calcium concentration decreases following the administration of the hormone. There is a similar decrease in cholesterol content of the blood. Carbohydrate metabolism is apparently unaffected by the synthetic adrenal cortical hormone. Low fasting blood sugar level is often as low or even lower after from 10 to 40 days of treatment. Extremely low carbohydrate values, 38 to 46 mg. per 100 cc. of blood, have been observed. Two hypoglycemic episodes occurred in 1 patient.

In all of the 13 cases treated with desoxycorticosterone derivatives, the blood pressure reached normal level from 2 to 4 weeks after instituting therapy and in 3 cases has risen to hypertensive levels—160/92, 160/110, 146/108 respectively In these cases no other etiological factor appeared to account for the increased systolic pressure.

Progesterone Therapy — Thirty mg of progesterone given for 7 or 8 days in 3 of the cases of Addison's disease, were entirely without either subjective or objective effect, according to Ferrebee, Ragan, Atchley and Loeb If the larger doses might have exhibited an effect is not known, but results do not correspond to the similarity of action of the 2 substances which have been reported in animal experimentation

Complications—Ten of the 13 patients developed edema of varying severity and transient puffiness of the face and ankles to massive anasarca Three patients developed respiratory distress, tightness in the chest, rise in venous pressure and a decrease in vital capacity. associated with x-ray evidence of pulmonary congestion One of these patients also developed striking dilatation of the right side of the heart, rapid increase in blood volume from 36 liters up to 45 liters developing also This patient required a restriction of fluid and salt to do away with this edema of adrenal cortical origin One case developed seri-

ous cardiac insufficiency, associated with a rise in venous pressure to 215 mm. of water, a systolic blood pressure of 160/110. At the time this occurred the patient was receiving only 15 mg. of desoxycorticosterone every other day and from 2 to 3 teaspoonfuls of salt in his The patient succumbed with a terminal pneumonia. Phlebotomy and limitation of salt and water were ineffective, except to reduce the venous pressure. Commenting as to the cause of cardiac insufficiency in 3 of the cases, the authors considered rapid and extensive increase in the circulating blood volume as a possible factor.

Subcutaneous Implantation of Desoxycorticosterone⁵ — After successful results had been obtained with the injection of the synthetic adrenal cortical hormone in cases of Addison's disease, the successful results obtained by Deanesly and Parkes⁶ from the subcutaneous implantation of estrogenic substance in ovarian deficiency cases as well as other successful reports on the implantation of testosterone and progesterone suggest the attempt to treat Addison's disease by the implantation of tablets of desoxycorticosterone acetate.

Thorn, Engel and Eisenberg⁷ implanted 200 mg of desoxycorticosterone in tablet form in adrenalectomized dogs and their results indicate that 1 mg. of this substance was utilized each day, whereas 1½ mg. was necessary to maintain a corresponding condition with daily injections.

Levy-Simpson⁸ reported his results in 4 patients in whom 200 mg. of desoxy-corticosterone acetate in tablet form were implanted subcutaneously. It was found that this quantity was sufficient to maintain an effective control of Addison's symptoms for about 3 months. The rate of absorption of the implanted hormone appeared to depend upon physical laws

and not upon physiological requirements except in the presence of unusual effort or infection.

Thorn and his associates^{3, 7} have also successfully used implantations of desoxycorticosterone acetate tablets in the treatment of Addison's disease. Their group is the largest so far reported and the results are most encouraging in every respect. They have also found that the body absorbs only the minimal amount required to control the deficiency existing.

Adrenal Cortical Hormone Therapy

Adrenal cortical hormone administration has been found effective in the treatment of burns by Einhauser,⁹ Wilson and Stewart.¹⁰ Desoxycorticosterone rapidly corrected the blood changes associated with body burns which begin within a few hours and reach the highest level in from 12 to 30 hours after the burns occur. The blood changes observed are a fall in serum sodium, a rise in serum potassium, blood chlorides, urea and nonprotein nitrogen and an occasional increase in corpuscular concentration.

The blood changes were rapidly corrected and circulatory failure was often dramatically, but not always, relieved by the administration of desoxycorticosterone. Two to 5 mg are administered, depending upon the severity of the blood chemical changes

Einhauser used vitamin C in conjunction with the adrenal cortical hormone.

Weinberg¹¹ reported a case of a female child, age 20 months, with myotonia congenita exhibiting complete loss of muscle power in the lower extremities and partial but progressive loss in the upper extremities. He administered ½ cc. of eschatin (adrenal cortical hormone) 3 times a week for 8 weeks with marked improvement. Improvement con-

tinued and at the end of a year the child could walk half a mile. The therapy suggested itself because adrenal cortex is antagonistic to quinine and the latter is specific for myotonia congenita which is the opposite state of myotonia congenita.

Adrenal cortex extract has been found to produce favorable results in child-hood asthma. Pottenger¹² reports improvement of the allergic state in 84 per cent and general improvement in 90 per cent of 50 patients.

PARATHYROIDS

Dihydrotachysterol in Parathyroid Deficiency

Rose and Sunderman¹³ state that dihydrotachysterol (A. T. 10) is an orally effective derivative of tachysterol which is one of several sterols derived from ergosterol by irradiation with ultra violet light. It produces an increase in serum calcium and a decrease in inorganic serum phosphorus concentration. Urinary calcium is increased and fecal calcium decreased. The ionized and the protein bound calcium fractions are reported to be increased by A. T. 10 administration. It was first used by Holtz¹⁴ in 1933 in the treatment of parathyroid tetany.

The work of Albright *et al* ¹⁵ indicates that the fundamental actions of vitamin D and A T 10 are similar in that they increase absorption of calcium from the gastrointestinal tract and increase excretion of phosphorus in the urine, the ratio of the latter to the former being greater with A. T. 10. Albright *et al.* conclude that the effect of A T 10 on the concentration of calcium and phosphorus in the blood is secondary to these fundamental actions and that the action of vitamin D is slower in onset and more prolonged than that of A. T. 10.

The preparation of A. T. 10 used clinically is an 0.5 per cent solution of dihydrotachysterol in sesame oil. Five to 10 cc. daily for 3 or 4 days usually causes a rise in the serum calcium in from 3 to 9 days after the initial administration of A. T. 10. The maintenance dose is usually from 2 to 6 cc. weekly.

Menstruation, pregnancy and increased physical or emotional activity require an increase in maintenance dose. It is reported that estrogen and androgen are antagonistic to A T. 10 and castration in women diminishes the requirement It does not cure lenticular cataract resulting from parathyroid tetany, but is said to prevent its occurrence.

Its chief therapeutic indication is in parathyroid deficiency, but it has been used in tetany of sprue, asthma, urticaria, hemophilia, and a variety of peripheral circulatory disorders.

The authors report on 5 postthyroidectomy cases with parathyroid deficiency ranging from 5 months to 13 vears duration who were administered A T 10 Their experiences confirmed the efficacy of A. T. 10 in severe forms of tetany due to hypoparathyroidism One patient in whom tetanic symptoms developed had been controlled by A. T Signs of hypercalcemia occur from the daily administration of 1 cc of A. T. 10 for 26 days Their experiences also confirmed the observation of other clinicians that a lack of correlation exists between the degree of hypocalcemia and the onset and severity of symptoms Their calcium fraction studies showed that the diffusible and the nondiffusible fractions of serum calcium share about equally in the use of concentration of the total serum calcium which follows the administration of A. T. 10. This finding is in disagreement with the findings of Holtz, et al., who stated

that the "colloidal" (nondiffusibles) was the first to increase during A. T. 10 administration.

"Dihydrotachysterol (A. T. 10) increased urinary excretions of calcium at the expense of fecal calcium."

The authors summarize the advantages of A. T. 10 as "its prompt and continued efficacy by peroral administration in maintaining normal concentrations of serum calcium and controlling symptoms without the necessity of dietary restriction (low phosphorus diet) or adjuvant therapy (calcium or vitamin D), as well as the small maintenance dose usually necessary. The principal objections to its use appear to be (1) its cost and (2) the necessity of guarding against hypercalcemia."

Tetany

Treatment with Dihydrotachysterol (A. T. 10)—Hurxthal¹⁶ comments that while mild parathyroid tetany can be controlled by oral administration of *calcium*, severe tetany does not always successfully respond to parathyroid hormone (parathormone).

A T. 10 (dihydrotachysterol) was used in 6 cases of chronic tetany and was found to control the severest type of case.

The method of administration varied. In severe tetany, 3 to 15 cc of A T. 10 were given daily for several days and then 1 to 2 cc. were administered daily. Blood calcium determination was done weekly at first and later from "time to time."

Calcium lactate administration was found to diminish the dosage requirement of A. T. 10 which acts by increasing calcium absorption from the gastro-intestinal tract

Since A. T. 10 in sufficient dosage produces hypercalcemia, the appearance of such symptoms as headache, nausea and general malaise in cases administered A. T. 10 requires its discontinuance until serum calcium has returned to normal.

PITUITARY

Acromegaly

Deep Roentgen-ray Therapy: Weinstein¹⁷ states that the treatment of acromegaly remains unsatisfactory. Hormonal therapy is indicated only when

there are no pressure manifestations on adjacent structures, such as the optic chiasma or the cranial nerves.

The patient, a white female, aged 40 years, he reports, exhibited evidence of an intracranial tumor and pituitary dysfunction. At age 24, menses ceased. Four years later, headaches appeared and facial and digital features of acromegaly appeared. About a year later she experienced weakness and nervousness and emotional instability appeared.

At the age of 28 she married and no pregnancies occurred

Beside the usual features of acromegaly, there was diffuse enlargement of the thyroid, lid lag, and exophthalmus, the left eye being more prominent. The blood pressure was 105/80. The fundi showed no evidence of intracranial pressure and the perimetric fields revealed slight, definite temporal constriction. The B. M. R. was plus 17 and the skull x-rays of sella turcica revealed marked enlargement and enlarged frontal sinuses.

It was decided to treat her by means of roentgen-rays. The treatment consisted of 20 milliamperes for 15 minutes through a ½ millimeter copper and 1 millimeter aluminum filter. This was delivered through an 8 centimeter portal at a distance of 50 centimeters. The roentgen-ray machine was a 200,000 volt apparatus, and the dose delivered was 300 milliampere minutes, amounting to approximately 800 to 900 "R" (with "back-scatter"). This treatment was given 4 times and the patient felt definitely improved.

The patient was readmitted to the hospital for the removal of a pedunculated sebaceous cyst of the left leg. Since her last admission she had experienced no weakness, irritability, headache or visual disturbance. The physical examination and laboratory data were essen-

tially unchanged, as compared with films of a year previous. Although there were no positive indications for further roentgen-ray treatment, she was given empirically a fifth and final treatment of approximately 1000 "R."

During the next 4 years the patient appeared in the outpatient department with minor ailments. She was working and apparently felt greatly improved. No visual disturbances had occurred and her sense of smell was normal. She experienced a return of libido and her menstrual cycle became re-established and was normal in all respects.

Two years later she complained of amenorrhea of 3 months' duration The uterus was found to be slightly enlarged A few weeks later she fell and a miscarriage occurred. Later that same year she was found to be pregnant and she was observed throughout a normal pregnancy. After a fairly difficult labor because of a posterior position, she was delivered of a normal male infant weighing 8 pounds and 10 ounces. The baby breathed spontaneously The puerperium was normal.

Still a year later, she was found to be essentially unchanged. There was no evidence of any progression of the pituitary disorder. At the time of her last visit to the clinic, no significant changes were noted.

Weinstein says that "When this patient was first seen there were signs both of tumor pressure and abnormal hormonal activity in association with enlargement of the hypophysis That prompt beneficient influence was exerted by the roentgen-rays was indicated by the rapid subsidence of headache, the disappearance of evidence of pressure on the optic tracts, and the return of a normal sense of smell. The late effects were remarkable and not altogether anticipated. There was no evidence of progressive change in the skeletal system. This we had hoped for. The return of the blood sugar and basal metabolic rate to normal levels was noteworthy. The re-establishment of the menstrual cycle was more than we expected and the occurrence of pregnancy seven years after irradiation of the pituitary region was quite unpredicted (It is true that we do not know that her husband has had normal spermatozoa all these years, and information relating to the present state of his spermatic fluid is not obtainable, since he refuses to co-operate with us)

"It is rather unusual, as judged from other reports, to have such striking im-

provement occur in acromegaly after roentgen-ray treatment. It should be remembered that spontaneous remissions are known to take place. However, the decided improvement observed in this patient followed so soon after the roentgen-ray treatment and was in such marked contrast to the progressive downward course of the disorder up to the time of treatment that a causal relationship between treatment and improvement seems highly probable. Moreover, if a spontaneous remission had occurred it seems likely that during the 10 years which followed some evidences of hypopituitarism might have become evident. Instead there seems to have been established a satisfactory balance. It appears that overactivity of the gland ceased entirely and the functions which had been suppressed prior to roentgen-ray treatment subsequently reached and maintained a normal level of activity.

"It is of interest that during the course of the pregnancy no abnormal functional activity of the pituitary was observed. The onset of acromegaly and the activation of the disorder during pregnancy have been noted."

"In the treatment of acromegaly uncomplicated by rapidly failing vision it may be desirable, in the light of our experience, to use deep roentgen-ray therapy in every instance whether or not signs of hypophyseal tumor are impressive. In some instances it may be then possible to avoid surgical treatment; in others, operative treatment may be delayed without detriment to the patient"

Diabetes Insipidus

Treatment by Insufflations of Powdered Posterior Pituitary Substance—Rutledge and Rynearson¹⁸ report on the successful use of posterior pituitary lobe extract by insufflation in 2 cases of diabetes insipidus

Case No. 1 was a Jewish woman, aged 39 years. The symptoms were of 8 weeks' duration and of acute onset. Her intake and output of fluid were about 18 liters per day and she drank incessantly and voided every 2 hours during the day and night. Pitressin jelly and ½ cc. of surgical pituitrin by hypo every 12 hours reduced the fluid intake and output to 6 liters, but abdominal cramps and menorrhagia prevented the continuance of pituitrin.

Nasal insufflation of a powder prepared from the posterior lobe of the pituitary was given every 3 hours during the day and at 1 and 3 A. M. The intake and output of fluid were reduced from over 12,000 cc. to an intake of 5150 cc. and an output of 6420 cc the day after instituting therapy. Under therapy the output gradually decreased to between 3000 and 4000 cc She was discharged the twenty-third day after instituting this therapy and 6 months later the output was about 2000 cc, with an intake of from 1700 to 2000 cc Insufflations are now taken every 3 hours during the day, the last dose being at midnight. She uses about 05 dram (19 Gm) of the powder per month.

A corresponding satisfactory result with a similar régime was obtained in a 56-year-old woman with a coexisting diabetes mellitus and diabetes insipidus.

SEX GLANDS AND HORMONES

Cryptorchidism

The subject of therapy for cryptorchidism is a timely one Rea¹⁹ beheves that about 10 per cent of human undescended testes are fertile and 82 per cent of those treated by orchidpexy have active viable sperm but never attain full normality. Cryptorchidism results from endocrine and nonendocrine anatomical conditions

Anterior lobe hypofunction is very likely responsible for most of the cases of true cryptorchidism. The true bilateral cryptorchid testis is undersized and the scrotum and penis are small.

Considerable controversy exists on therapy in cryptorchidism.

- 1. Conservatism or expectancy for spontaneous descent.
 - 2 The indications for surgery, and,
- 3. The age when therapy should be instituted, the method of administration, and the hormone product advocated.

The plea for natural forces is advocated by Drake²⁰ and, most convincingly, by Johnson.²¹ Opposed to this conservatism is the report of Gordon-Taylor²² that in 50 cases of neoplasm of the testes, 15 occurred in retained testes.

The report on cryptorchidism by Johnson covers a 7-year period, during which he examined 31,609 members of boys' clubs. He observed an incidence of 172 per thousand in boys from 7 to 17 years of age. He cites Army statistics of 2 cases per thousand in the recruits examined, a difference of 15 cases per thousand.

Of the total 544 cases of undescended testes, 246 were bilateral. Seventeen of these were associated with Frohlich syndrome, as compared to 11 cases of Frohlich syndrome with unilateral undescended testis in a total of 298. Frohlich syndrome was more frequently observed without cryptorchidism. In only 5 cases, 7 to 9 years, were endocrine substances injected and all were failures

Spontaneous descent and a normal testes occurred in 300 instances bilateral 162, unilateral 138. Between the ages of 11 and 13, the testes descended spontaneously in 174 cases. This is the age of adolescence and the age when organotherapy shows its best result, with 68 per cent cures as compared with 32 per cent failures.

Of 544 cases, 63 more recent cases had not been re-examined and, with an established 29 per cent average turnover loss of members yearly, a loss of 157 is computed. The expected number of un-

descended testes would be 220 and actually it is 217. He concludes, "Do not operate for undescended testes before the sixteenth year unless operation is indicated by some associated condition."

"Glandular therapy before the age of puberty is useless and harmful and at the age of puberty is unnecessary. The greatest number of spontaneous descents occurs between the ages of 11 to 14. After 14 years of age there is a marked fall in the incidence of spontaneous descent."

There is a unity of opinion that all cryptorchid cases associated with anatomical anomalies should be operated. The difficulty is in determining when anatomical processes prevent testicular descent. Spence²³ states the superficial inguinal ectopic testes should not be treated because it has no natural pathway. He states that this type of cryptorchid testes is more palpable than the inguinal, is not displaceable upwards into the inguinal canal, but it may be displaced to the femoral region and lateral to the neck of the scrotum and not into it as will an inguinal testes.

The choice of therapy in cryptorchidism lies between:

- 1 Pregnancy urine extract (P U E) (A P L),
 - 2 Anterior pituitary extract injections,
- 3 Oral administration of anterior pituitary and thyroid, and
 - 4 Male hormone injections

The possibility of A. P. L substance producing antihormone in the unsuccessfully treated cases is negated by the reports of Dorff²⁴ and Saphir ²⁵ A more important point is that P. U. E activity differs widely from species to species, and what is true of an animal is not necessarily true of the human. The ovary of the immature macaque monkey does not react to A. P. L. substance,

whereas it will to a human pituitary extract containing prolan.

Thompson, et al.'s,26 results in cryptorchidism in a carefully controlled series show only 20 per cent cures with A. P. L. substance as compared with an average of 61 per cent cases of cures in the literature. They stress the importance of excluding cases of pseudocryptorchidism or migratory testes. Thompson infers that treatment should usually be limited to 2 months with a daily dosage of from 100 to 1000 rat units.

The best results with P. U. E. occur during the pubertal years. However, the 2 unfavorably therapeutic responses (beside the failure and return of the testes to the former site) have been reported in critical studies in which P. U. E. were administered—edema of the scrotum or testes; return of the testes to former size and atrophy after discontinuing therapy, and evidence of premature puberty with abnormal hypertrophy of the phallus. The effect of this precocious state on the general body mass has not been defined.

Gonadotrophic Pregnant Mares' Serum Hormone

In 1930 Cole and Hart²⁷ found that the injection of crude serum of pregnant mares into mature animals produced what might be termed precocious development of their immature gonads, indicating its gonadotrophic activity all animals injected with pregnant mares' serum, the testes, seminal vesicles and prostate showed measureable increase in size, and injected immature female animals exhibited enlarged ovaries with mature follicles and corpora lutea and, as a result of the induced follicular maturation and estrin production, the uterus developed and a positive estrus reaction was detectable in female rats.

During the past few years an extensive experimental investigation has been made of this substance in various species of animals, and in 1938 Hartman²⁸ found that the administration of pregnant mares' serum produced ovulation in anovulatory monkeys.

The active principle of pregnant mares' serum is a gonadotrophic substance, so far as can be determined, of chorionic origin. It is dissimilar in its action on the ovary to pregnancy urine gonadotrophic extract, but very similar to the anterior pituitary gonadotrophic factor discovered by P. E Smith²⁹ in 1926. The danger of anaphylactic shock from the serum proteins of the pregnant mare's blood prevented its earlier use in human patients. In 1937 Cartland and Nelson³⁰ overcame this serum protein problem and obtained a highly purified preparation of this new gonadotrophic substance, the product being a dry, white, water-soluble powder. According Davis and Koff,31 "it is apparently a peptide and is not soluble in the usual fat solvents used for the isolation of estrogenic hormones."

In hypophysectomized rats the injection of pregnant mares' serum gonadotrophic hormone produces a follicular stimulation equal to that obtained with castrate or menopausal urine gonadotrophic extract, which is 2-plus compared to the 1-plus of anterior pituitary gonadotroplic extract or pituitary implants and has a luteal and an ovulatory value equal to anterior pituitary gonadotrophic extract, which does not occur with castrate or menopausal urine gonadotrophic extract. It exhibits no degenerative changes in the ovary, such as hemorrhage and atresia of the follicles, whereas the pregnancy urine gonadotrophic substance produces this to a 1-plus degree

Assay—This is based upon an increase in ovarian weight, or follicular

maturation, occurring in immature female rats. The rat unit of gonadotrophic principle is not standardized as yet by the international council. The individual manufacturers describe their rat unit as follows:

Anteron: The unit in which the potency of anteron is expressed is one-tenth of the amount required to produce an average 5-fold increase in ovarian weight in 5 immature rats of the Wister strain weighing between 35 and 45 Gm. 96 hours after the first of 6 subcutaneous injections, given 3 each day on 2 successive days.

Gonadin: A rat unit of this preparation is that amount which, 96 hours after a single injection, will cause development of an average of 3 to 10 follicles or corpora lutea in a group of 5-, 21-to 23-day-old female rats.

Gonadogen: The rat unit is defined as the minimum total dose of hormone which, administered to 21- to 23-day-old rats weighing 35 to 45 Gm., in 3 equal subcutaneous injections at daily intervals, will produce at autopsy, 96 hours after the first injection, a mean ovarian weight of 65 mg., which is 4 to 5 times that of the controls.

Spence, Scowen and Rowlands³² had previously demonstrated that the prolonged administration to human patients of a gonadotrophic extract prepared from human pregnancy urine did not evoke the formation of inhibitory substances (antihormone). When such a gonadotrophic substance (anterior pituitary, pregnancy mares' serum) obtained from 1 species is injected into another animal species, these antihormonal bodies cause a refractiveness of the gonads to its stimulatory effect, according to Meyer and Gustus.3.3 Rowlands and Spence34 studied this refractive reaction in 9 patients with undescended testes, who were injected with a gonadotrophic substance

prepared from mares' serum in which 1 mg. was equal to 80 international units (150 mg. being equal to 1 rat unit).

Three patients were injected daily for 12 weeks with 6, 12, and 13.5 mg., respectively. Three patients were injected with 18 mg. and the 3 remaining patients were injected with 36 mg. twice weekly for 12 weeks. The antigonadotrophic activity of the serum of all the patients was negative prior to therapy. The serum of most of the patients showed antigonadotrophic activity about 6 weeks after daily or twice weekly injections of the pregnant mares' serum gonadotrophic extract The antigonadotrophic concentration, on the whole, increased as therapy was continued but, in the main, ceased to increase after stopping therapy. Two of the cases receiving 36 mg. twice weekly continued to rise for another 4 weeks. The titer of antigonadotrophic activity rose to the level where its inhibition effect against the gonadotrophic substance was estimated at being sufficient to counteract 4.5 Gm or as being 5 times more than the total amount (0.864 Gm) of gonadotrophic substance injected during the course of treatment

After maximal antigonadotrophic activity was reached, there was at first a rapid fall and subsequently a gradual loss of activity. However, 3 or more months' posttherapy an antigonadotrophic activity was still present.

Investigation of the species specificity antisera reaction revealed that antigonadotrophic activity of the serum produced by pregnancy mares' serum extract injections was ineffective against human anterior pituitary and human pregnancy urine gonadotrophic substance. Some proof of this was also obtained clinically.

The clinical results obtained in the 9 cases of cryptorchidism treated for 12 weeks with pregnancy mares' serum

gonadotrophic extract in the dosage previously mentioned were negative. No improvement in the position of the testes was noted. The administration of human pregnancy urine extract to the patients produced successful results in 3 patients

Two explanations for the unfavorable results are possible; either:

- 1. Pregnancy mares' serum gonadotrophic extract is ineffective in cryptorchidism, or
- 2. Refractoriness to the extracts develops and makes ineffective the subsequently injected extract

Indications—Pregnant mares' serum gonadotrophic hormone is indicated in amenorrhea and sterility. The objective of both cases is to produce maturation of immature follicles so that the follicle will form, thus producing the formation of the ovarian follicles, estrogenic substance, the development of the ova, and, last, the development of the corpora lutea and progesterone

To provide results of this order, therefore, the natural anterior pituitaryovarian interrelationship must be simu-Accordingly, the method lated administration recommended is that the preparation be given in a series of small doses, 10 units daily or every other day until 60 units are administered, with the last dose being administered on the twelfth day of the calculated cycle of the 28 days. If desired, the duration of series injection may be shortened so that 20 to 30 units of the total of 60 units are administered on the twelfth day.

In the original clinical research work of Davis and Koff,³¹ they administered from 50 to 90 units of pregnant mares' serum intravenously from the second to the twenty-eighth day. Most patients received 60 units and it was administered in the majority of patients from the seventh to the sixteenth day of the cycle

Their studies of the effect of pregnant serum on the human ovary of a woman with normal ovarian activity and periodic ovulation observed at the time of operation and by microscopic slides is: "We have been led to believe that the process of ovulation in the human being extends over a period of several days or longer, during which time the follicle slowly reaches maturity and ultimately, some time in the new cycle, ruptures and discharges its ripe ovum." Their observation of the effect of pregnant mares' serum, intravenously administered on the human ovary, causes them to state: "We can thus theorize that this substance is capable of causing rapid follicle growth and that these follicles rupture, release their ova and are converted into corpora lutea, all within the space of 24 to 36 hours."

Their conclusions from their studies are:

- "1 It has been possible for the first time to produce ovulation in women by the intravenous use of a gonadotrophic hormone derived from serum of pregnant mares.
- "2. This hormone has been isolated in such an advanced state of purity that its administration by the intramuscular or intravenous route is devoid of danger, provided that suitable safeguards are established
- "3 Biologically, this gonadotrophic hormone resembles extracts and implants of the anterior lobe of the hypophysis but differs chemically and biologically from all other gonadotrophic substances heretofore studied
- "4 These experimental ovulations have provided the earliest human corpora lutea yet described
- "5 Clinically, this gonadotrophic hormone should prove efficacious in the therapy of patients in whom follicle growth and ovulation are at fault"

Hall³⁵ reports his results with pregnant mares' serum in a series of 135 patients who were classified as follows:

- 1. Menstrual disturbances,
- 2. Genital hypoplasia,
- 3. Sterility

A number of patients could be classified in more than 1 group, as sterility and hypomenorrhea or subjective signs of estrogen deficiency with genital hypoplasia, dysmenorrhea, or oligomenorrhea.

The preparation used was gonadin, a rat unit (Cole and Saunders) of this preparation being the amount which, 96 hours after a single injection, will cause development of an average of 3 to 10 follicles or corpora lutea in a group of five 21- to 23-day-old female rats. On the basis of experimental evidence in animals (rat, ewe, sow, cow, mare), in which ovarian weight rather than body weight is the determining factor, it is estimated that from 600 to 1000 rat units would be required to stimulate the ovary of the human female

The majority of patients treated in this series received 200 rat units (Cole and Saunders) of equine gonadotrophic hormone on the seventh, eighth and ninth days following the onset of menstruation. The average duration of therapy was 4 months

Estrogen therapy, 2 to 10,000 rat units of estradiol benzoate, was administered every 3 to 5 days during the postmenstrual and intermenstrual phase over a period of 1 or 2 cycles in cases of amenorrhea, hypomenorrhea, oligomenorrhea, genital hypoplasia and some cases of sterility prior to instituting the equine gonadotrophic hormone

Effect of Pregnant Mares' Serum Injections in 135 Cases of Menstrual Disorders — Primary amenorrhea, 4 cases, ages 21 to 25 years, were treated for 6 months, 1 cure, 2 improved.

Secondary amenorrhea, duration 1 to 2 years Six cases were treated for from 4 to 6 months with 4 cures and 2 improved

Hypomenorrhea, 101 cases, about onethird of whom were under 30 years of

age, the condition being present for from 6 months to 15 years. Of the total number, 54 per cent were cured and 34 per cent improved, with the younger age group showing a 2-to-1 greater percentage of failures.

Oligomenorrhea, 33 cases of a duration from ½ to 3 years. There were 55 per cent cured and 25 per cent improved.

Menometrorrhagia (menorrhagia and metrorrhagia) due to persistent follicle, there were 16 cases treated with 75 per cent cured and 19 per cent with improvement.

Dysmenorrhea, 32 cases of a duration of from ½ to 15 years, 69 per cent of those treated were cured and 25 per cent were improved. Twelve patients have been free from symptoms for a time as long as 10 months after discontinuing therapy.

Genital hypoplasia; of 17 cases, 47 per cent were cured and 35 per cent improved. The latter required therapy to maintain the improvement. The failures were highest in cases where there was external and internal genital hypoplasia.

Sterility — Forty-three cases, duration 3 to 17 years. There were 14 cases with apparently normal menstruation, yet with a history of sterility in 50 per cent of the cases from 7 to 10 years, 71 per cent of the 14 cases became pregnant. In 8 cases of hypomenorrhea of from 5 to 18 years, pregnancy occurred in 62 5 per cent. In a similar number of dysmenorrhea cases, pregnancy occurred in 75 per cent.

The evidence of pregnancy following pregnant mares' serum was low in oligomenorrhea (28 per cent in 7 cases) and in menometrorrhagia (33 per cent in 3 cases).

Of the 3 cases of amenorrhea, 2 of which were secondary and 1 primary, no pregnancy occurred.

Concerning the failures of response to therapy, Hall is of the opinion that ovaries which are small, white and atretic do not respond to this or any other form of therapy. This type of ovary was subsequently observed at laparotomy in some of the cases in this series which exhibited negative results from equine gonadotrophic serum.

L. F. Hawkinson,³⁶ in his discussion of Hall's paper, stated that he obtained comparable results with pregnant mares' serum in 93 cases of menstrual disturbances and sterility. He administered larger dosages of pregnant mares' serum, the majority of patients receiving 200 Cole-Saunders or 20 Cartland units for 5 doses, beginning the fourth or fifth day after the onset of menstruation The injections were given daily or every other day, the last dose being administered prior to the assumed date when ovulation should occur.

S. A. Payne³⁷ also reported the use of still larger dosage, spread over a longer period of time, in many cases of menstrual disturbances. The cases received 200 to 400 Cole-Saunders rat units 3 or 4 times a week for several weeks.

The Mare Serum Hormone in the Treatment of Endocrine Dysfunctions in Women—R B Kennedy and C. F. Shelton³⁸ administered intramuscularly 50 units of gonadogen to 10 cases of amenorrhea, hypomenorrhea, and oligomenorrhea There were some negative results but the majority of therapeutic results from gonadogen was favorable. The injections were given at monthly intervals about the twelfth day of the cycle for from 3 to 8 months

In their opinion, pregnant mares' serum therefore appears to be the most available and potent gonad-stimulating substance to be used in hypogonadal states in the female. The foreign protein

content of the preparation appears to be inconsequential as a material producing serum reactions.

Editor's Note: Its use in male hypogonadal states is yet to be evaluated. The recent report by Rowland and Spence is discouraging in 2 directions; first, it was noneffective in cryptorchidism, and, secondly and more important, is the fact that it produces in large amounts, when injected in humans, its specific antihormone factor.

Treatment of Hypogonadism in the Adolescent Male

Webster³⁹ recognizes 2 types of hypogonadal adolescents, first, those exhibiting delayed puberty in whom spontaneous recovery will occur, and, second, those evidencing hypogonadism which persists into adulthood.

Hypogonadal cases requiring therapy fall into 3 types:

- 1 The Frohlich.
- 2. The eunuchoid, and,
- 3. The nutritional type due to some severe disease in which there is an arrest of genital development

The purpose of replacement therapy in the definitely hypogonadal adolescent is desirable, not only to correct the genital underdevelopment but also to prevent the psychic trauma which these individuals undergo because of their sexual hyperplasia

A bov aged 14 years presented a penis 114 miches long and small soft testes. After 6 weeks of testosterone therapy—25 mg twice a week—the penis was 314 miches long, the testes firm and slightly larger, and the prostate previously not palpable was barely palpable. There was a coarse growth of hair on the legs, secondary genital hair was present and the voice had deepened.

A boy aged 13½ years under similar therapeutic régime had similar penile, prostate and secondary sexual development. The testosterone therapy failed to increase the size of an atrophic left testicle, the right testicle was

absent. He had had at age 10 years a bilateral hernioplasty, at which time the left cryptorchid testes was placed in the scrotum. The right testis was not found.

A boy aged 14½ years, slightly obese with prominent mammae and marked hypoplastic genitals, penis and testes, both being about ½ inch long, was administered 5 mg. of testosterone propionate 3 times weekly for 8 weeks with no effect. The dose was increased to 25 mg. and in 3 weeks there was a definite increase in the size of the scrotum, the testes appeared to be firmer and larger, and the penis was slightly enlarged. At the end of 6 months he exhibited a heavy growth of axillary and pubic hair; the penis was 2½ inches long and the testes 1½ inches long; the prostate was palpable. His general appearance was distinctly more masculine.

A boy aged 17 years exhibited the nutritional type of general underdevelopment, associated with marked primary and secondary sexual deficiency. The urinary androgens were diminished. He was given 25 mg. of testosterone propionate 3 times a week for over four months. There was a marked increase in his general state, a gain in height of 1½ inches, well developed secondary sexual hair growth along with an increase in the size of the penis from 2 to 4 inches and an increase in the size of the testes and prostate gland.

The sequence of the changes observed in hypogonadal adolescent cases administered testosterone propionate are:

- 1. Appearance of pubic and axillary hair,
- 2. Penile and scrotal growth, increase in size of prostate,
- 3. Deepening of voice and growth of beard

It was thought that in 3 of the 6 cases treated that there was an increase in the size of the testes. While weight increase occurred, the patient looked less obese due to the loss of regional—mammary and abdominal—obesity.

Concerning dosage, Webster is of the opinion that 5 mg of testosterone propionate is inadequate. Twenty-five mg dosage is required to produce anatomic development of the penis, scrotum and

prostate This growth, as well as the psychosexual feature, may be maintained by 10 mg 2 or 3 times a week.

No instance of excessive libido was noted during the administration of the 25 mg. testosterone propionate. In the opinion of the author, a greater number of cases will require therapy and observation to obtain more definite data on the clinical dosage.

Clinical Use of Synthetic Male Sex Hormone

Turner⁴⁰ presents the results of 2 years' experience with the synthetic male sex hormone, testosterone propionate, in the treatment of hypogenitalism, impotency, symptoms of sexual decline, benign prostatic hypertrophy, and gynecomastia

Fifteen cases were treated of which 11 were cases of hypogenitalism, 2 cases of impotency and sexual decline, 1 case of prostatic hypertrophy, and 1 case of gynocomastia

The therapy administered in the above cases was testosterone propionate, 10 to 25 mg 2 or 3 times weekly. Effective results were estimated in hypogenitalism by the desired effect on voice change, growth of hair, increased size of the phallus, production of erection with emissions, development of libido and potentia, and in prostatic hypertrophy by clinical improvement.

Case No. 1 is an 11-year-old boy with small testes and penis. Injection of 10 mg of testos-terone propionate 3 times a week for a period of 4 weeks definitely increased the size of the penis.

Case No 2 is a 40-year-old male eunuchoid, with a penis the size of an 8-year-old child, atrophic scrotum and no palpable testes. Antuitrin-S and prephysin therapy in 1933 and 1934 failed to improve his genital state. Injections of 25 mg of testosterone propionate were given 3 times weekly. After 6 injections he reported having erections and emissions and after 12 injections his first intercourse occurred. His voice pitch deepened and his penis.

enlarged, and in 13 weeks there was, beside the enlargement of the penis, increase in sexual urge and energy and hair growth over the entire body. After 18 weeks, when a total of 1100 mg. of testosterone had been administered, he was given injections of pure sesame oil for 6 weeks. He then complained of not feeling so well, libido decreased, turgescence and fullness of the scrotum decreased, and sexual intercourse was increasingly difficult. On resuming the testosterone propionate injections, he again improved

The marked enlargement of the penis following the administration of male hormone injection was illustrated by case photographs in this and in case No. 3, who was 26 years and presented a high pitched voice, subgenital development—penis, 4 cm long, infantile scrotum, right testes not palpable-lack of facial and axillary hair and practically no pubic hair Libido and potentia were absent. Open epiphyses were present in the ulna. He also failed to respond to antuitrin-S (11,500 r u.) in 1936 The therapy instituted here was 10 mg of testosterone propionate injected 3 times a week. After 18 injections there was a perceptible increase in the size of the phallus and slight scrotal development. The prostate gland previously unpalpable was noted as palpable but very small After 16 weeks of therapy, he showed a weight gain of 21 pounds, improved appearance and normal demeanor Daily erections now occurred, but the ejaculate The left testicle contained no spermatozoa was one-third larger and occupied a lower scrotal position and the right testes was palpable in the upper scrotal region. Pubic hair increased but facial hair had not developed

Case No 5 was a male, white, aged 16 years, whose chief complaints were obesity and subgenitalism—infantile penis but approximately normal-sized testes situated in the upper scrotal region, and deficient public hair growth Antuitrin-S therapy caused descent of the testes but no growth of the penis. Testosterone propionate injections, 10 mg 3 times weekly, caused enlargement of the penis. The number of injections was reduced to twice weekly because the scrotum was becoming of the adult (serrated) type. Three hundred and thirty mg of testosterone propionate were administered in 3 weeks.

Case No 6 is a boy aged 9 years whose bilateral cryptorchidism had responded to A P. L injections but whose penis and scrotum remained infantile. Six injections of testos-

terone propionate, 10 mg. twice weekly, caused erections to occur 2 and 3 times a week and 25 mg. twice a week produced almost continuous priapism. A rest period of 2 weeks was given and therapy was resumed on the original schedule and was continued for 7 weeks, at which time the penis was normal in size but the left testis remained small and atrophic.

Three other children of pre-pubertal age were reported. In a 7-year-old child a dose of 5 mg. twice weekly was administered. After 80 mg. were injected there was a remarkable penile growth, frequent erections, but no change in size or descent of the small right testis and the left was cryptorchid.

In a boy 9 years old of the Frohlich type, penile growth occurred following testosterone propionate injections—10 mg twice weekly—but the penile growth response was slower than that observed in the other cases and regressed in size after stopping therapy.

The 2 cases of sexual decline and impotentia responded favorably to 5 mg of testosterone propionate twice weekly.

Case No 15 is a 23-year-old white male whose chief complaint was bilateral gynecomastia with well developed hirsutism and normal genitals. Female sex hormone assay of urine was normal and male hormone was a low normal (286 i u). Twenty-five mg of testosterone propionate injected twice weekly for 13 weeks failed to reduce the size of the breasts which were virginal glandular tissue type with well developed areola and nipple

In commenting on the favorable response of male hormone therapy in the group of 15 patients, the author cites the improved body changes, increase in hair growth, enlargement of the laryinx, and improved weight distribution. The small sized penis increased in size in all patients and was associated with an increase in public hair. There was evidence of testicular growth in some patients. The hypoplastic prostate increased in size but remained underdeveloped for the age. Augmentation of sexual prowess was observed in all cases.

The symptoms associated with sexual decline were nervousness, irritability, insomnia, apprehension, fatigue, and gas-

trointestinal disturbances, all responding favorably to male hormone therapy, with an equal improvement in the mental attitudes of all patients.

No untoward side effects were noticed except transient swelling and soreness of the breast which was observed in 5 cases

Hypogenitalism in the Male

Treatment with the Gonadotrophic Principle of Pregnant Mares' Serum

-There is general agreement of the fact that the anterior pituitary-like hormone from pregnancy urine and placenta are of value in the treatment of some types of hypogenitalism and cryptorchidism. Kunstadter⁴¹ states that the urinary and placental extracts are not true pituitary gonadotrophic hormones since they fail to prevent atrophy of the gonads in the hypophysectomized animal The gonadotrophic hormone of mares' serum does not act directly on the tubular tract (uterus and vagina) but exerts its stimulating effect on the ovaries producing follicle and corpus luteum development, which is followed secondarily by estrous changes in the tubular tract, characteristic of the ovarian hormones which are produced in the ovary under stimulation by the gonadotrophic hormone.

The group consisted of 14 boys between the ages of 6½ and 14¾ years. The material used was pregnant mares' serum hormone, gonadogen. From 10 to 20 U. U. were administered intramuscularly 3 times weekly. The course of treatment varied from a minimum of 2 weeks to a maximum of 18 months.

The results of treatment were judged by the growth of the genitalia, appearance of secondary sex characteristics and descent of undescended testes. Of the 14 patients who began treatment, 2 had to be eliminated because of severe local reactions. Four patients (3313 per cent)

showed marked improvement, as indicated by marked growth of genitalia with or without the appearance of secondary sex characteristics and complete descent of undescended testes. The length of treatment ranged from 9½ months to 18 months, with the ages of the patients ranging from 11 to 143/4 years. A second group of 4 patients (33½ per cent) responded with moderate improvement, marked by moderate growth of the genitalia, partial or complete descent of the undescended testes Length of treatment in these cases ranged from 11 to 21 weeks with the ages of the patients ranging from 11 to 13½ years. One case showed little improvement with slight growth of the genitalia. No improvement was shown by 25 per cent of the cases (3 patients) These patients ranged in age from 6½ to 11 years Of the 12 patients, 8 or 66% per cent showed evidence of definite improvement after treatment with mares' serum

Four of the 14 patients showed pseudo-cryptorchidism in which the testis was freely movable and could be manually placed into the scrotum, but retracted immediately. There were 7 cases of true cryptorchidism in which the testes could not be placed into the scrotum manually. All but 1 of the patients with bilateral cryptorchidism showed, in addition, definite endocrine disturbance Response to treatment was most satisfactory in this group. None of the 3 patients with unilateral cryptorchidism showed evidence of endocrine disturbance and in only 1 of these patients was there definite response to treatment as evidenced by partial descent of the testis These results bear out the author's previous contention that cryptorchidism is most satisfactorily treated with hormones in those patients that have a coexisting endocrine disturbance.

Enlargement of the penis does not occur often until after growth of the testes and in all probability is secondary to the production of male hormone by the stimulated testes. There was no change in the distribution of fat nor weight loss in any of the patients treated. The obesity of some patients increased out of proportion to the rate of growth during the period of treatment

Four patients ($28\frac{1}{2}$ per cent) showed local reactions.

The results are similar to those obtained with prolan and anterior lobe extracts, although with the doses of mares' serum used, the duration of treatment was more prolonged. It is difficult to estimate a correct dosage as the response of any hormone varies in different individuals and in different age groups

Percutaneous Absorption of Male Hormone

Foss⁴² reviews the numerous reports of animal experiments which determined the fact that male hormone is absorbed into the blood stream through stratified epithelium and that locally applied to capon's comb it is 200 times more effective by munction than parenterally

The report of Moore is cited which states that 50 mg. of testosterone and testosterone propionate in 1 ounce of cream, rubbed into the backs of castrated male guinea pigs and rats, maintains the accessory reproductive organs

Foss treated 3 cases—a 38-year-old postpubertal eunuch, a 60-year-old male who had bilateral orchitis and numps and who complained of impotency, and a youth of 18 with delayed puberty, with an ointment containing 25 mg. of testosterone propionate per gram The ointment was dispensed in a tube and the patient applied daily about 1 inch of the ointment, approximately 18 to 25 mg of testosterone propionate, to the skin of the thighs and abdomen. The skin was cleaned prior to applying the salve This patient had been previously treated with injections of testosterone propionate and observed that whereas impotency recurred 5 to 6 days after receiving an injection of testosterone propionate, the inunction of testosterone propionate in the above strength maintained his potency and also made him conscious of the feeling of impending erections, even to a point of daytime inconvenience. Beneficial results were observed after 8 days of daily inunction of male hormone and continued during the 30 days of daily therapy, but disappeared in about 1 week after discontinuing the inunctions of male hormone ointment,

The 60-year-old eunuchoid was similarly treated at first daily and then twice daily. After a month's therapy, there was a strong growth of hair on the axilla, thighs, arms and abdomen. Hair had been absent from these parts for 25 years. In 2 months there was a growth of hair on the chest and nightly erections and desire for coitus. In 3 months he again married and continued the twice daily application. He is able to enjoy coitus several times a week An injection of about 100 mg. of testosterone propionate has been given monthly since adopting the inunction application of testosterone propionate. When difficult intromission, due to incomplete turgescence, is experienced, increasing the dose of ointment corrects this situation.

Case No 3, a youth of 18 with delayed puberty, exhibited a feminine type of pubic hair, high-pitched voice, and a left testicle which was smaller than the right. The penis and scrotum were fairly well developed. He had received 3500 mg of testosterone propionate by injection during a 10-week period without satisfactory results. After a lapse of therapy for 8 weeks, he was given 2100 mg. by injection in the next 6 weeks. The voice deepened but frequently lapsed into the highpitched tone. During the last 112 weeks of the second injection period, I inch of male hormone ointment was applied twice daily over the larynx and this was continued for 21/2 weeks after the injections were discontinued. At the end of this period his voice became fixed at the desired low tone. He had received a total of 5000 mg of testosterone propionate by injection in 24 weeks with no marked effect in stabilizing his low-pitched tone, as compared with 450 mg of ointment which brought about fixation of the voice at the desired normal tone The author states, "This method of giving male hormone is effective and simple, but a larger dosage is required than when the hormone is given by injections.

"An ointment containing 25 mg. of testosterone propionate per Gm. in 2-Gm. collapsible tubes is recommended for practical use as the most efficient means of percutaneous androgen therapy at present available."

Testicular Deficiency

The Treatment with Testosterone Propionate — The study is concerned with the urinary androgens in the normal male, in testicular deficiency and after injections of androgens. McCullagh⁴³ states that the effect of the injected androgens has also been studied on penile growth and function, the influence on secondary sex characteristics, semen production, and spermatogenesis, epiphyseal closure and urinary excretion of the injected androgens.

The normal average of urinary androgens per 24 hours in normal men (in 20 cases) as determined by bio assay (capon comb growth) is 35.1. Koch⁴⁴ reported an average of 30 in 20 assays on men between 24 and 34 years of age with a low of 16 and a high of 72.

Six cases of severe hypogonadism, 1 case of functional hypogonadism and 1 adult castrate were studied in this report

Testosterone propionate injections in males are followed by an increase in the quantity of urinary androgens. This determination of urinary androgens indicates in a general way the dose and the frequency of administration of androgen required to establish normal urinary androgen values in cases of testicular deficiency.

After the injection of 10 mg, of testosterone propionate, the urinary androgen may fall in 3 days to the original negative assay. When larger doses are injected, the complete excretion consumes a longer time. When the amount of injected hormone is sufficient to estab-

lish normal urinary androgen content, it is usually found that all the symptoms of testicular deficiency disappear, but it is apparently necessary to maintain this androgenic urinary content to establish normal development of the anatomic parts, the testes excepted. The testes have not exhibited a definite increase in size in most cases following the administration of male hormone therapy.

Secondary sexual characteristics are advanced to normal. Epiphyseal closure has not been advanced above the normal rate by testosterone propionate therapy.

Effect of Testosterone Propionate on Spermatogenesis in the Human

Rubinstein and Kurland⁴⁵ report a continuation of the previous study of testosterone propionate on spermatogenesis. Eight normally constituted adults were studied. Of this number, 5 had normal ejaculatory findings, 1 was oligospermic, 1 was azoospermic and 1 showed hypoactive spermatozoa.

Six cases received 3 intramuscular injections of testosterone propionate weekly in doses of 5, 10 or 25 mg and the other 2 patients were injected twice weekly. Samples of ejaculations were studied mostly at weekly intervals

One case had an obstruction of the ejaculatory ducts, testicular puncture showed motile spermatozoa. All other patients responded to therapy. The 5 mg dose of testosterone propionate caused an increase in sperm content in the normal ejaculate but larger amounts, 25 mg, were required in the oligospermic Cessation of therapy led to a return of a normal count either promptly or gradually. Large dosage, 25 mg, usually diminished the sperm count which returned to normal after stopping therapy

Case No. 8 showed an increased viability of the spermatozoa In no case was

the genital or hair growth increased. Small doses temporarily stimulated sexual desire, whereas large dosage led to a transitory period of increased libido which, in spite of the treatment, disappeared entirely

The suppression of spermatogenesis in normal individuals by the administration of 25 mg. of testosterone propionate may be due to the depression action of the excess androgen on the pituitary while 5 mg. may stimulate the germinal epithelium; it seems then that the male hormone produced by the interstitial cells can stimulate another tissue, the germinal epithelium, of the same gland

The authors conclude: "Testosterone propionate, when administered to normally constituted adult males in 5 mg intramuscular doses 3 times weekly, led to an increase in spermatozoal counts This increase was maintained throughout the duration of treatment in all but I case in which, in spite of treatment, the elevated count receded to normal after several weeks. Increasing dosage to 25 mg per injection in the normal adult led to a suppression of spermatozoal output. Whether counts were elevated or depressed during treatment, cessation of therapy led, either promptly or after several weeks, to the return of normal figures. The oligospermic individual required more hormone to raise his count than did the normal. A patient with ejaculatory duct obstruction failed to respond to treatment. A childless patient displaying 50 per cent hypomotile sperm responded with an increase in motility. His wife became pregnant after 2 months of treatment.

"There was neither increase in genital size nor increase in crines pubis. While small doses of the hormone temporarily stimulated libido, large doses depressed it"

The Male Climacteric

Werner⁴⁶ states that the onset of sexual decline occurs later in the male sex (48 to 52 years) than in the female sex (40.8 years).

Not all cases of sexual decline, irrespective of their sex, exhibit symptoms of the climacteric. The symptoms complex of the male climacteric correspond to that experienced by the female. They may be classified as in women as nervous, circulatory and general in distribution. "Among the more prominent symptoms may be mentioned intense subjective nervousness, definite emotional instability characterized by irritability, sudden changes in mood, decreased memory and ability for mental concentration, decreased interest in the usual activities, a desire to be left alone, and depression and crying They may have hot flushes, which may be accompanied by profuse perspiration or to be followed by a chilly sensation There may be tachycardia and palpitation, even while lying in bed, and tachycardia, palpitation and dyspnea on moderate effort, vertigo with or without change of position, scotomas, tinnitus, numbness and tingling in the extremities. fatigability and disturbed sleep"

"The neurocirculatory symptoms, such as hot flushes and suddenly increased perspiration, chilly sensations, vertigo, scotomas, tachycardia and palpitation, and the numbness and tingling occur irregularly, they may be of frequent occurrence for a few days and then there may be a short period of relative freedom, only to recur."

"The symptoms which are mental and psychic, such as irritability, changes in mood, decreased memory and concentration, loss of interest, restlessness and depression and crying, are usually more constant."

"The climacteric disturbance may be so severe in some men that they become

despondent and develop a psychosis with thoughts of self-destruction. It is very probably why many men have committed suicide and no one could understand the reason for their having done so. That men have involutional melancholia can be confirmed by psychiatrists, for most institutions caring for mental patients have had these cases."

A report of 2 cases is made:

Male, aged 50, complaining of nervousness, excitability, irritability, and lately mental depression. Severe hot flashes, numbness, and tingling of the extremities, tachycardia, palpitation, dyspnea, fatigability, vertigo, occipitocervical aching and frontal headaches 6 or 7 times a month. Recent decreased memory and loss of concentration. The genitals were normal.

Therapy was 10 mg of testosterone propionate injected 3 times weekly. After 4 weeks of therapy his depression had disappeared and the subjective symptoms were markedly improved. The symptoms recurred 3 months after discontinuing the testosterone propionate injections. The diagnosis was male climacteric.

Case No 2 was a male, aged 42, who was a partial castrate with atrophy of the remaining testicle. The above gonadal condition was incidental to hernia operations. At the first operation, the testis was removed because of its atrophic state and at the second operation an orchitis developed, and 6 weeks later he had a complete loss of sexual potency, experienced nervousness, restlessness, hot flashes, perspired profusely and was depressed. Memory and concentration were decreased. Recently he has been greatly fatigued and has had daily frontal headaches. The diagnosis was castrate, left side, testicular atrophy, right side.

The administration of 10 mg 3 times a week for 4 weeks produced relief of all his subjective symptoms and coitus was accomplished. Reduction of the frequency of injections produced a proportionate reduction in the number of erections

Three injections of 10 mg of testosterone propionate are required to maintain a normal state and discontinuance of therapy brought recurrence of the original clinical state

Male Hormone Therapy — Dunn⁴⁷ states that the male sex may exhibit evi-

dences of gonadal insufficiency during the various ages of life. The adult male, during the fifth and sixth decades, can also manifest a climacterium symptomcomplex similar to the female climacteric.

Irritability, sudden mood changes, crying, tendency to seclusion, depression, headaches, suboccipital tension, lack of interest in social and business life, lack of mental concentration and energy are among the prominent nervous and mental symptoms of the male climacteric.

Vertigo, hot and cold flashes, excessive perspiration, chilliness, coldness of dependent parts, numbness, tingling, sharp or dull extremity pains, tachycardia and palpitation are among the neurocirculatory symptoms.

The general symptoms are chiefly weakness, lack of endurance and physical strength, and a feeling of inadequacy or incompetency in carrying on former activities or engaging in new duties Responsibility either hangs heavily on the shoulders or is evaded.

Gonadal insufficiency states may occur because of genital underdevelopment in the maturing and adult male, and are well exemplified in the Frohlich syn-The diminished physical and mental energy and aggression, the petulance, irritability and anger tantrums, the frequent trend toward stealth and deception and, occasionally, more serious practices, present major social and therapeutic problems.

Under more general types of body underdevelopment, there exist cases exhibiting marked retardation in physical growth and hypoplasia of the testes. The most unhappy type of gonadal hypoplasia and deficiency is the eunuchoid. Other cases are observed in the atrophy of the testes following mumps; infections of the testes, as in tuberculosis;

anatomic or pathological disorders, and castrates.

The extent and degree of the complex clinical picture are dependent upon: (1) The amount of the specific hormone deficiency; (2) the duration and degree of its progression; (3) the extent of disturbance of endocrine interrelationships; (4) the tissue and blood chemical responses to be affected.

The 15 cases treated were classified as follows:

Eunuchoidism—5 cases Testicular Hypoplasia-2 cases Testicular Atrophy, following mumps-Secondary to anterior pituitary deficiency—

(a) With infantilism, and (b) With cryptorchidism-2 cases

Climacteric-4 cases

The male hormone was administered hypodermically; 30 mg. to 150 mg of testosterone propionate were given weekly. Therapy was concluded in most cases at the end of 12 weeks and dosage was gradually reduced as the symptom picture improved, or signs of sexual activity were made manifest. The ointment preparation—containing 2 mg per Gm. of testosterone propionate—was administered in dosage of 33 mg, per week, and continued for 3 to 4 months.

The therapeutic result was, in general, a relief of symptoms proportionate to the dosage administered. The effects, when obtained, were either general and specific, or symptomatic Under general effects, we include weight gain in thin individuals, improved facial appearance and color, and the replacement of the abnormal youthful appearance by a countenance expressing more virility and stamina

The measured production of the facial hair growth, and particularly the secondary genital hair, should be considered essentially as a specific effect of male hormone therapy, but this specific effect is usually overshadowed by the improved psyche and an appreciable but not prominent increase in libido. The increase in physical energy and ability to sustain physical effort over a greater period of time is marked.

The relief of head pressure pains, numbness, tingling and neuritic extremity pains, and the disappearance of the emotional outbreaks allow home and social life to be resumed without fear of unpredictable aggravated attacks.

Rapid therapeutic effects, even by hypodermic administration of the testosterone propionate, are not always obtainable. Dunn believes that proper sedation has a field of application during the early acute clinical states, but as soon as adequate male hormone therapy has been accomplished, the sedation should be reduced and, later, discontinued.

Male hormone therapy is a replacement therapy instituted to gain control of a deficiency state, and present experience shows it to be effective in relieving the nervous and mental symptoms associated with the hypogonadal syndrome. However, as the therapy is one of replacement, symptoms may recur when the deficiency state recurs.

Benign Prostatic Hypertrophy

Treatment with Testosterone — Strohm. Edelson and Merryman⁴⁸ report their conclusions obtained from a study of the results observed in 25 cases of benign prostatic hypertrophy treated with testosterone propionate

The dosage used was 5 mg. of tes tosterone propionate twice weekly. The case reports are of men in or about the sixth decade of life.

The authors report that fair results are obtained in early prostatic hypertrophy; partial results in a hypertrophy of moderate duration; poor results in the advanced cases.

(Editor's Note: The results obtained in this series of cases rather parallel those obtained by Pugh⁴⁹ in a similar study of the subject.)

Effect of Testosterone on the Histology of Prostatic Enlargement in Man—Sharpey-Schafer and Shackman⁵⁰ report that favorable results have been reported as being obtained by the administration of androgens in prostatic enlargement. The successful results have been judged by the favorable effect on the symptoms complained of by the patient, by estimations of the reduction in residual urine, and the diminished size of the prostate as gauged by rectal examination and cystoscopy. Reference is made to Clark's⁵¹ view of the results of therapy in the disorder, that when there is a minimum of instrumentation and no therapy administered there is great variability in the course of the disease and often there is apparently spontaneous cure.

The dosage of testosterone propionate recommended by the various authors as effective in prostatic enlargement has varied from 1 to 40 mg. daily.

The authors' report concerns the case of a laborer, age 53 years, with increased daily and nightly urination and hematuria of a few days' standing. The size of the prostate was determined at operation on October 17, 1938, when the bladder was opened, at which time a biopsy of the middle lobe was obtained.

From October 18 to November 20, 1938, 100 mg of testoterone propionate in oil were injected daily, a total of 3400 mg being administered. On November 21 the bladder was again opened and it was judged by palpation that the prostate had diminished one-third in size. The prostate was enucleated, with difficulty, and examined histologically. The pathologist's report on the prostate tissue, both before and after testosterone propionate therapy, was that "The 2 specimens show no significant differences in their histological structure."

In commenting on the operation and histological findings and the therapy, it is stated that the dosage of testosterone propionate administered in this case is greater than has been given by most workers and in view of the suprapubic drainage having been performed, no definite conclusion can be made as to which therapy diminished the size of the prostate gland

Male Breast Hypertrophy

Hormone Therapy — Hoffman⁵² states that while male breast hypertrophy may occur at all ages, it most frequently appears at puberty and adolescence The glandular mass, which is benign, occurs beneath the areola and nipple, is tender, and usually measures from 1 to 5 cm in diameter. The breast hypertrophy undergoes regression in the majority of cases, with only 1 out of 7 persisting after 20 years of age

Factors suggesting a disturbed hormonal influence in this unusual activity of the male breast are:

- 1 Its high incidence during puberty, adolescence, and the age of sexual decline
- 2 Its regression as male adulthood is reached, and
- 3 The fact that hypertrophy of the breast may accompany malignancy of the testes, testicular atrophy, or castration

In 1935 Hoffman treated 6 patients with hypertrophy of the breast by injections of anterior pituitary-like substances. Injections were given weekly for periods of from 2 to 10 months. No consistent results were obtained, and the therapy was abandoned.

The author reports the results obtained with the administration of testosterone acetate and testosterone propionate in 28 male patients, from the ages of puberty to the eighth decade, who had unilateral or bilateral hypertrophy of the breast.

The first cases received 5 mg of testosterone acetate twice weekly, no harmful effects being observed from the dosage. The cases later received 25 mg. twice a week when it became evident that the male hormone neither produced testicular damage nor the arrest of sexual pubertal changes.

Complete regression of the hypertrophy of the breast occurred following the administration of testosterone propionate and testosterone acetate in 50 per cent of the cases and there was a 75 per cent regression in 9 other cases treated. In the main, the response was relatively rapid in the first 4 weeks. An average of 28 injections was required and after 1 month's treatment, the regression was approximately 50 per cent completed. After from 2 to 5 months' therapy, sometimes there was a persistence of a small nodule which frequently disappeared after discontinuing therapy. In at least 2 cases there was a recurrence of the breast hyperplasia, these recurrences disappearing after injections were resumed

In 2 cases there were complete failures, the breast mass even increasing in size. One, a 13-year-old, received injections twice weekly for 10 months, with the only result that his subgenital development, which was that of a 9-year-old boy, became normal.

There were 2 instances of undescended testicles and in neither instance did descent of the testes occur

A total of 31 cases of breast hypertrophy in males was observed. In 3 of the youngest cases, however, there was evidence of regression when examined and they were not treated; spontaneous regression of the breast hypertrophy occurred in these cases.

Chronic Mastitis

Treatment with Testosterone Propionate — Of the 24 patients treated with painful breasts (chronic mastitis) observed by Spence,⁵³ 16 were treated

with testosterone propionate with "dramatic relief of pain in most cases; diminution of the nodules, although effected in some patients, was less striking."

Their ages ranged from 19 to 52 years, the majority being between 30 and 40 years.

The dose employed was 25 mg. of testosterone propionate twice a week. In cases where no relief occurred it was increased to 50 mg. twice a week and later to 100 mg. 2 or 3 times a week for as few weeks or many months as required. The total dosage varied from 2000 to 3000 mg. and in others from 100 to 500 mg

The effect of therapy on the breast pain varied. A few injections of 25 mg. relieved some, whereas others required 50 to 100 mg doses. Two thousand milligrams during 20 weeks administered to 1 patient failed to relieve the pain. One patient received inadequate treatment due to the increased growth of hair on the face.

Of the 16 patients treated, there were 12 who complained of pain in the breasts; of these, 8 were relieved, 2 were improved, and 2 unrelieved.

Of the 12 patients with lumps in the breast, improvement occurred in 8 and in 3 the mass disappeared. In 2 of the latter spontaneous disappearance was a possibility. One patient received 2925 mg, in the 5-month period required to cause disappearance of the large lump in the right breast.

The administration of 2000 mg and in another patient 2075 mg caused suppression of menses and the breast lumps were unaffected. Doses of 100 mg usually caused amenorrhea. Menstruation was suppressed in 3 patients, in 2 with 50 mg, twice a week, in 3 with 100 mg, twice a week, and in 2 with 100 mg, 3 times a week.

Increased hair growth on the face, limbs, and trunk appeared in 5 patients and necessitated cessation of the therapy. Hair growth appeared on the face as early as 4 weeks after instituting therapy. In 1 patient examined for hypertrophy of the clitoris, it was found to be enlarged.

As a control, 24 patients received olive oil injections to observe the effect on breast pain. Thirteen patients experienced relief from the pain.

Inhibition of Lactation During Puerperium by Testosterone Propionate

Kurzrok and O'Connell⁵⁴ report on the administration of testosterone propionate in cases where suppression of lactation during the puerperium is desired Twenty-one patients received a total dosage of from 50 to 150 mg. of testosterone propionate, divided into 2 injections per day or more, to control the discomfort of the full lactating breast and dry them up.

In 19 cases the results were considered excellent, particularly when 25 mg, dosage was administered. Complete relief generally follows the second injection which is usually given 8 hours after the first. In 48 hours there is usually total relief of the breast engorgement and there was no incidence of recurrence after 40 or more mg of testosterone propionate had been administered.

In summation the authors say

"Twenty-one cases of early lactation during the puerperium were treated with testosterone propionate, for the purpose of inhibiting lactation. Usually the inhibition of lactation by the generally used therapeutic measures, and especially in their absence, is associated with pain, tenderness, engorgement, and lumpiness of the breasts. Such breast symptoms

require considerable nursing care and are very distressing to the patient. Testosterone propionate, in doses of 25 mg., usually relieves such symptoms in about 24 hours without the addition of any other therapeutic measures. The hormone is injected twice a day, intramuscularly, in the buttocks A total dose of 100 mg. may be given within 48 hours, although if complete relief occurs after the second or third dose, no additional dose need be given. The puerperium was not otherwise affected by the hormone, and there were no unpleasant after-effects"

Testosterone Propionate in Functional Bleeding

The administration of testosterone propionate to 25 cases of functional uterine bleeding rapidly controlled the excessive bleeding in all but 2 cases, according to Geist, et al 54a. The clinical improvement was associated with definite changes in the endometrial picture as determined by examination prior to, during, and after treatment.

Pelvic pathology was excluded in all but 4 cases in which small intramural involuta were present.

The diagnoses were:

- 1 Menorrhagia, 13 cases,
- 2 Menometrorrhagia, 5 cases,
- 3 Menorrhagia, with polymenorrhagia, 7 cases

Half the patients were between the ages of 40 and 49 years, the remainder being from 34 to 39 years of age. The average duration of the bleeding was 2 years, the limits being 2 months and 10 years.

After a trial with low dosage, 45 to 200 mg per month, without effective results, the total dosage was increased, in certain cases up to 1000 mg. The highest dosage for any single case was 2150 mg. over a period of 3 months.

All but 20 of the cases treated responded favorably to the testosterone propionate; however, amenorrhea of from 2 to 5 months' duration occurred in 14 of the 25 cases treated. Normal menses were established in 9 cases, in 2 the menses were delayed, and in 2 others regular but scant menses occurred

Four cases developed mild facial hirsutes. One case developed a facial acne and in 3 cases slight coarsening of the voice was noted.

Except in 1 case of hirsutes, all the undesirable effects regressed with cessation of therapy.

Metabolism of Testosterone

In 1938 Callow⁵⁵ reported that a definite increase in urinary androgens occurred when 50 to 100 mg, of testosterone propionate were administered weekly A rise of urinary androgens from 9 i u. to 81 i. u occurred in a castrate male receiving 50 mg, of testosterone propionate daily. This is, nevertheless, a low percentage of recovery, since 50 mg of testosterone propionate is equivalent to 3500 i. u of androgenic activity. The loss of activity might result from inactivation of testosterone, to conversion to less active androgens, or to a combination of both.

In 1939, Callow, Callow and Emmens⁵⁶ reported an increase of the 17-ketosteroids in the urine following the administration of testosterone. This increase in hormone-like substance was in part due to large amounts of androsterone, dehydroandrosterone, and an inactive isomeride-edi-etio-cholanolone.

Cook and Hamilton⁵⁷ in the same year reported that oral administration of testosterone causes an increase in the androsterone content of the urine. They reported a rise of the excretion of androgen in the urine from 21 1 u. per day to 500 i. u. per day in a case where

60 mg. of testosterone were administered orally daily for 15 days and 120 mg. orally daily for the next 7 days.

Attention is directed to the reports of Steinach and Kun,⁵⁸ Callow, Callow and Emmens,⁵⁶ demonstrating that the administration of testosterone propionate and androsterone benzoate is followed by a 3-fold rise in the estrogenic activity of the urine.

Parkes⁵⁹ pointed out that the gross androgenic activity of the urine does not measure the level of the hormonic activity of the testes.

The article states, "It is reasonably certain that administration of testosterone may appear in the urine as estrogen, as a different androgen, or as a biologically inactive substance, and it seems likely that the endogenous androgens, presumably mainly testosterone, will be similarly modified before excretion. Moreover, the excretion products so far identified are not specific to men, since normal women seem to secrete as much androsterone as normal men, and epitactiocholanolone also occurs in the urine of women.

"This conclusion greatly complicates the problem of diagnosis of the level of testicular activity by examination of the urine, whether by biological or by chemical methods so far elaborated"

Stilbestrol

This synthetic compound, 4.4-dihydroxy-alpha-beta-diethyl stilbene, known as stilbestrol was discovered by Dodds⁶⁰ and his coworkers in 1938, and has been found to have estrogenic qualities similar to that of the natural estrogenic hormone. This substance has been widely used in English and in continental clinics and is now procurable in England for general use. Under the new United States Federal regulations, it must be tested clinically by approved and ex-

perienced clinicians before it can be offered for sale. Subsequent to this, it must be approved by the Council of Pharmacy and Chemistry.

It has been known that this substance causes considerable gastric distress, nausea and vomiting in a relatively high percentage of cases, according to most observers. This evidence of toxic effect is being investigated with particular reference to this toxic damage in the human. The patients administered Stilbestrol who have developed nausea. vomiting and abdominal pain, quickly discontinue it on their own initiative. Besides the toxic or untoward symptoms reported, this writer has observed in 3 young females to whom the drug had been administered in a dosage of from 1 to 5 mg. daily for from 14 to 16 days, excessive development of the breast which became firm, almost tense, and sensitive, but more particularly intense pigmentation of the areola After discontinuing therapy, the hyperplasia of the breast regresses but the pigmentation of the areola only partially disappears.

Three preliminary reports of the administration of Stilbestrol have been published by the Council of Pharmacy and Chemistry⁶¹ who conclude, "that its use by the general medical profession should not be undertaken until further studies have led to a better understanding of the proper function of such drugs."

The Fate of Estrogens in the Body

Diethylstilbestrol has the same physiological activity as the natural estrogenic hormones which, as quoted by Wenner and Joel⁶² is to,

- 1. Induce a proliferation of the endometrium:
- 2 Abolish the deficiency manifestations of the climacteric,
- 3 Stimulate the growth of a hypoplastic uterus;

- 4. Abolish the pains of dysmenorrhea, and
- 5 Prevent or inhibit lactation

Stilbestrol has, according to an annotation in the Lancet,63 little chemical resemblance to the natural estrogens dissimilarity in their chemical behavior in the body has been found by S W. Stroud⁶⁴ and B. Zondek and F. Sulman,65 Stilbestrol remains deposited and is slowly absorbed from the site of the injection, whereas estrone is rapidly absorbed and, because of this, the esters of estrone and estradiol have been used to prolong its action Secondly, after stilbestrol has entered the circulation, its compounds, stilbene and dyphenylethane, derivatives, are recovered from the urine in comparatively large amounts, as compared to the rapid mactivation of estrone and the recovery in the urine of its less active breakdown products. It thus appears that the body mechanism is incapable of mitigating the action of the synthetic estrogenic agent stilbestrol and there is produced in the body a much more highly estrogenic substance, 4-4'dihydroxystilbene

The article concludes with the statement, "We are getting under the guard of the body mechanism and giving it a compound against which it has not developed an adequate defense"

Indications for Estrogen Therapy

Estrogen Deficiency—Geist and Salmon⁶⁶ report that 2 methods are now available in the objective determination of both the presence of an estrogen deficiency and the efficacy of the therapy. These methods are:

- 1 The human vaginal smear, and,
- 2 The gonadotrophic hormone excretion

Papanicolaou and Shorr⁶⁷ have demonstrated that the human vaginal secretions, after the menopause, exhibit certain cytologic characteristics Because of

the complications involved in this technic, the method is not practical for office or clinic use.

Geist and Salmon have developed a simple, rapid, objective method of determining whether a patient is suffering from an estrogen deficiency and, by taking smears periodically while the patient is receiving estrogenic hormone treatment, can estimate objectively the effectiveness of the therapy. Their method consists of determining the urinary gonadotrophic hormone output, an indirect method of determining the presence of an ovarian deficiency By continuing the gonadotrophic hormone assays while estrogens are being administered, the adequacy of the estrogen dosage can be ascertained when the gonadotrophic hormone vanishes from the urine, indicating inhibition of the hyperactive hypophysis This method is time-consuming and requires the facilities of a laboratory. The cytologic characteristics of the vaginal smear and the gonadotrophic hormone excretion in the menopause have been correlated so that it may be assumed that when the vaginal smear shows a complete estrogen effect after therapy (Reaction IV), the gonadotrophic activity of the hypophysis has probably been reduced to a normal level. In addition, endometrial and vaginal biopsies have been used as indicators of the degree of ovarian deficiency

In this study estradiol (Progynon-DH Schering), estradiol-benzoate (Progynon-B, Schering), emmenin (Ayerst, McKenna, and Harrison), estradiol-dipropionate (Ciba) and diethyl stilboestrol (Squibb, Ayerst, McKenna, and Harrison) have been used

If the vaginal smear indicates advanced estrogen deficiency, the patients should be started immediately with large doses (10,000 R U 3 times weekly). Smears should be taken at 3-day inter-

vals and the dosage diminished to 2,000 R. U. 3 times weekly when the smear shows a full estrogen effect (Reaction IV). It is important to continue the intramuscular injections for at least 4 weeks after a full estrogen effect and complete subsidence of symptoms have occurred, to prolong inhibition of the hypophysis and establish a store of estrogens in the body If small doses are given, the hypophysis becomes hyperactive when therapy is discontinued In cases where there are moderate symptoms and where the smear shows a slight degree of regression, 4000 R. U. 3 times weekly may be adequate. If there is no improvement of the condition within 1 week, the dosage should be increased.

Where therapy is discontinued and the symptoms recur, it is wise to put all such patients on a maintenance oral dose of estrogen, immediately after the cessation of the injections, in order to keep them symptom-free If these patients are given a concentrated course of estrogens for 4 weeks (10,000 R U, estradiolbenzoate, 3 times weekly), they can thereafter be kept free of symptoms with a normal estrogenic smear, on 1200 to 1800 oral units of estradiol per day Geist and Mintz⁶⁸ have shown that the natural menopause cases respond satisfactorily, also, to emmenin in adequate doses Geist and Salmon⁶⁶ found that the flushes and other annoying symptoms are kept under control with 1000 Collip units, 3 times daily, as maintenance therapy

Senile Vaginitis—The smear in the cases of senile vaginitis revealed the most advanced degree of estrogen deficiency. Best results are obtained by giving 10,000 R U 3 times weekly, supplemented with estrogen suppositories every night (2500 R U estradiol per suppository, every night). Improvement was noted

within 48 hours and symptoms were completely controlled at the end of a week or 10 days. Regeneration is still incomplete, however, and cessation of the therapy causes a recurrence of the symptoms in a few weeks It is advisable to continue treatment for 4 weeks after complete subsidence of the symptoms. Thereafter, 1 vaginal suppository (2500 R. U.), twice weekly, is sufficient to keep the vaginal mucosa in a normal physiologic state.

Pruritus Vulvae—Cases of pruritus vulvae require intensive constitutional estrogenic treatment, fortified with local inunctions with an estrogen ointment. The usual dose is 200 R U. estradiol per Gm. of lanolin base (Progynon-DH Lanol), applied nightly. After the usual course of estrogens, administered intramuscularly, the ointment should be continued for 6 months. Should evidence of regression appear in the smear, another course of intramuscular injections should be given.

It has been noted in several patients that following local treatment with estrogens the vulva loses its shrunken appearance and the skin and labia become fuller and softer. These changes are particularly striking in the cases that show early kraurotic changes. The tendency to fissuring disappears and the patients volunteer the information that the skin does not feel as dry or as hard as formerly

Functional Amenorrhea — Some cases of functional amenorrhea show an excessive production and excretion of gonadotrophic hormone, while there appears to be none in other cases. The nature of the hormonal derangement in functional amenorrhea is in need of clarification. In the cases with estrogen deficiency, the dosage should be approximately 200,000 R. U, estradiol-benzoate, intramuscularly, during the first month

of treatment. The estrogens were supplemented with progesterone during the second 2 weeks, giving 20 mg. per week. If uterine bleeding does not occur, treatment is discontinued for a week. Usually this bleeding will occur 5 to 8 days after cessation of treatment. Immediately after the cessation of bleeding, estrogen therapy should be recommenced, reducing the dose during the second month by 25 per cent. This is repeated for 3 successive months, reducing the dosage each month by approximately 25 per cent. The progesterone is continued as during the first month. Some cases with advanced atrophy of the endometrium require as much as 500,000 R. U. during the first month to induce uterine bleeding.

Oligomenorrhea—In cases of oligomenorrhea small doses of estrogens are frequently helpful if the basal metabolic rate is normal. Usually 10,000 R. U twice weekly for 2 months, in addition to 20 mg. progesterone per week during the second 2 weeks, reducing the dose by half in the third and fourth months will produce definite improvement.

Gonorrheal Vaginitis in Children—The results with estrogens in cases of gonorrheal vaginitis in children are very striking. The estrogen can be administered hypodermically in doses of 2000 R U. twice weekly; by mouth, in doses of 1800 oral units per day; or in the form of suppositories (2500 units each might) Treatment should be continued until the smears become repeatedly negative, which usually happens in 3 to 4 weeks.

Miscellaneous Conditions — Estrogens are also of value in treating urinary frequency and dysuria, atrophic rhinitis, breast adenosis, dysmenorrhea, migraine, and involutional psychoses.

Estradiol-dipropionate has been used in a series of 14 cases with varying de-

grees of menopause symptoms. The dosage varied from 1 to 5 mg. 2 or 3 times weekly, given intramuscularly in sesame oil. The number of cases comprising this study were not sufficient to determine whether this estrogenic compound possesses any virtues that would make it preferable to other estrogens.

Stilboesterol was used in a series of 38 menopause cases. The hormone was administered intramuscularly, in doses of from 1 to 5 mg. 3 times weekly, in oily solution and, by mouth, in doses of 06, 3, and 5 mg. per day (tablets, Squibb-0.1, 1, and 5 mg. each); and capsules (Ayerst, McKenna, and Harrison—1 mg. each). It was found that stilboesterol produces characteristic estrogen smear changes similar to those produced by the physiologic estrogens Estrogen smear changes may appear, after 10 to 20 mg., in 4 to 7 days It was very difficult to administer stilboesterol orally because of the untoward reaction of most of the patients. Stilboesterol does relieve the vasometor symptoms resulting from estrogen deficiency and it stimulates epithelial proliferation of the atrophic vaginal mucosa and probably also of the endometrium

The authors found that the effect from a given amount of implanted crystalline hormone is more prolonged than from an equal amount of hormone when injected in solution in oil Several patients have been maintained for more than 6 weeks with a single implantation of 4 to 5 mg of the pure hormone (estradiolbenzoate), which is equivalent to a total dosage of 24,000 and 30,000 R U respectively.

Clinical Use of the Female Sex Hormones

Winterton⁶⁹ sets forth the following definitions. Estrin is the generic name for the estrogenic hormones; estradiol

is the hormone secreted by the ovarian follicles; estrone is the product excreted in the urine. Estrin and estrone are rapidly absorbed and rapidly excreted, but the benzoate ester of estradiol is not readily destroyed and, therefore, has a more prolonged effect. Since estradiol and estrone are of known chemical composition, they are measurable by weight and converted into the international unit (i. u.), 1 mg. being the equivalent of 10,000 i. u The international benzoate unit is equal to 5 i. u. Corpus luteum hormone is measured in international units, 1 mg. representing 1 i. u.

The menopause is interpreted by the author as a stage of life when there is a transition from active sexual life to senile life, during which process there is a fall in the estrin level of the body. The patient may suffer from the menopausal symptoms until the body accommodates itself to this new and lower level of estrin values.

"It is in these cases that estrin can be given to help the patient over the change. The dose of estrin varies with the severity of the symptoms. The flushes can be controlled in many cases with 1000 i. u. a day, in others as much as 30,000 i. u. a day are given, but injections are rarely required."

"It is often necessary to give very high doses. Sometimes 50,000 international benzoate units given by injection twice weekly may be necessary and may be combined with local treatment by estrin pessaries This is continued until there is a response, usually in 3 to 6 weeks. The trouble may recur, in which case the treatment may be repeated. The estrin acts by increasing the nutrition of the vulva and vagina and the amount of glycogen in the epithelium, thereby enabling it to overcome the infection."

Estrogenic Therapy of Vaginitis— The treatment of vaginitis with estrogenic substance is well confirmed by numerous workers. Mazer and Schechter⁷⁰ reported the results obtained in 118 cases of vaginitis treated with estrogenic substance administered by injection and vaginal suppository.

They also report on the assays of the various estrogenic substances, a matter of prime importance in therapy and all too frequently disregarded. They determined by assays that 1 Gm. of theelin (estrone) yielded 1,000,000 R. U.;1 Gm. Progynon D.H., 10,000,000 R. U. (estradiol); and 1 Gm. Progynon B (estradiol benzoate) 5,500,000 R. U. of estrogenic activity.

Oral estrogenic therapy was found ineffective in treating vaginitis Therapy should be maintained for 8 weeks, according to their findings Cures are dependent upon creating a temporary maturity state of the vaginal mucosa and reducing the pH of the vaginal secretion to a point below 6 The injection every other day for 8 weeks of from 500 to 1500 R. U. of estrogenic substance gave the best results in cases treated by hypodermic with recurrence in 10 per cent of 78 cases Vagınal therapy gave the best results three of 34 cases nightly administered a vaginal suppository containing 200 R. U. of Progynon B had a clinical and bacteriological cure Follow-up of 26 cases revealed no recurrences.

The undesired side effects observed from the administration of estrogenic substance in young females were. Pubic hair growth (7 per cent); breast hypertrophy (26 per cent), uterme bleeding (10 per cent), all of which were of a temporary nature and were experienced less frequently with vaginal estrogenic therapy Breast hypertrophy usually disappears in 1 month.

Production of Breast Growth in the Human Female—MacBryde⁷¹ was

able to demonstrate that by injection of from 150,000 to 350,000 i. u. of estrone or estradiol benzoate per week, active growth of mammary tissue could be produced in patients who had no visible or palpable breast tissue. Unit for unit, estradiol benzoate was much more effective than ketohydroxyestrin (theelin) (estrone) in producing breast growth When patients were administered an alternate daily injection of 1 i.u. of progesterone and from 20,000 to 50,000 i u. of estrone or estradiol benzoate, breast growth was more rapid than that produced by the estrogenic hormone alone.

Concurrently with the breast development, the vagina and uterus exhibited the characteristic estrogenic effect on these tissues Clinically there was relief from the hypogonadal symptoms of hot flashes, and emotional instability, there was improved metabolism and subsequent weight gain

After allowing the estrogenic stimulated breast growth to regress until the major portion had disappeared, munction of a hydrous wool fat and petroleum base ointment containing 5000 i ii per gram of estradiol or estradiol benzoate was applied to the regressed breasts. Each day 5 (m) of omtment was applied over an area of 1 breast and nipple of approximately 10 cm in diameter, the other breast was used as a control and only an ointment base was applied Definite and considerable breast growth occurred in the treated breast, also there was relief of symptoms, uterus and vaginal estrogenic response occurred as with injections of estrogenic substance The estrogenic ointment was unit for unit more effective in producing breast growth than the injections of the estrogenic substances The breast growth is usually observed after 10 days of munction to the treated breast. As therapy

is continued the untreated breast gradually enlarges to the size of the treated. Regression of the breast development occurs after stopping therapy.

The author has expressed the opinion that this therapy is at present an experimental study and should not be applied generally to cases with breast hypoplasia or absent breasts until further studies are made.

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GASTROENTEROLOGY

Edited by Henry Leroy Bockus, M D

CHRONIC GASTRITIS

By WM A SWALM, MD, and L M Morrison, MD

Gastroscopy—B B Crohn⁶ attempted to correlate the histology of the stomach with the gastroscopic observations in chronic gastritis In resected portions of the stomach from a series of ulcers, most of which were benign, he draws

attention to the fact that often there is no parallelism between the gastroscopic diagnosis and the histologic picture Frequently, when hypertrophic gastritis is seen with the gastroscope, little morphologic changes are discernable. On the

other hand, he has found that the gastroscopist may report a normal gastric mucosa, and vet a rather advanced infiltration with round cells and plasma cells and eosinophiles may be noted. However, he does admit that there is a group in which the parallelism is in accord, where a gastritis is seen grossly and an infiltrating congested mucosa is observed microscopically. The Reviewers, however, would like to emphasize and stress from personal experience the meeting of 3 cardinal requirements in such a study as that of Crohn: (1) Gastric tissue should be especially fixed and prepared immediately upon its removal, otherwise changes occur which render study unrehable. (2) Correlation of gastritis studies should be attempted in their "pure" state, that is, in the absence of associated and local organic disease as ulcer and cancer (3) The amount of surgical trauma, cutting, clamping and instrumentation to which the stomach is subjected during surgical resection is considerable and cannot be overlooked in a study such as Crohn reports However, he points out the important fact that one of the greatest drawbacks in the whole issue is the lack of knowledge regarding what constitutes a normal mucosa and what changes can be expected in the mucous membrane of individuals in the later decades of life.

Crohn reiterates the belief that gastrius can have a psychogenic etiology, as the Reviewers have considered in previous communications. These nervous influences may produce a pathological physiology with resultant functional and hyperemic congestive states in the gastric mucosa. They are then expressed clinically in such symptoms as dizziness, depression, weakness, sense of fullness and insomnia. Crohn believes that Gutzeit may well be correct in assuming that gastrius is the most common of human

ailments since hasty eating, bad dentures, excessive condiments and the ingestion of too hot or too cold foods is a wide-spread habit. Crohn analyzes a group of 9 cases of antral gastritis—verified surgically—with a definite symptom complex resembling peptic ulcer. He found, however, that the epigastric pain and distress with anorexia and heartburn are usually more continuous than in ulcer; periodicity is absent and the course is more rapid and severe. He found that high normal hyperacid secretory curves accompany this ulcerlike type.

Bank and Renshaw² gastroscoped an additional 65 patients with peptic ulcer to make a comparative estimation of gastritis to radiographic 6-hour gastric retention. They found the incidence of gastritis to be independent of retention. A syndrome of duodenal ulcer was present in 26 per cent of chronic superficial gastritis cases Diarrhea was found in 16 per cent unaffected by the acid content, and loss of weight occurred in 46 per cent Massive hemorrhage was present in 1 instance, and occult blood in the stools in 42 per cent Foci of infection were found in 86 per cent of cases, and in the majority of patients, multiple foci were present. Alcohol and tobacco, in the opinion of Bank and Renshaw, appeared unimportant as etiologic factors

Pathology—In a symposium on gastritis at the Mayo Clinic, H. E Robertson^{20, 21} presented his pathologic observations on the development of gastritis into ulcer or carcinoma as follows (1) Tiny hemorrhages occur in the gastric mucosa from "undue excitement, stimulating liquors, overloading the stomach with food, fear, anger or whatever depresses or disturbs the nervous system" (Quotation from William Beaumont's observations on Alexis St. Martin in 1847) (2) The inevitable result of these

hemorrhages is an ulcer, that is, destruction of the mucosa in the region of the ruptured capillary. This ulcer may be extremely superficial and very small and the repair perfect. (3) Such an area, however, may be more vulnerable to future hemorrhages and more serious ulcerations. (4) Healing may then be inhibited to such a degree that a chronic ulcer results and causes the known ulcer syndrome. (5) The cause for nonhealing of these ulcers is unknown. Possibly alterations in the quantity or quality of the protective coat of mucus has oc-Possibly the central nervous system controls the factor. Robertson then explains the genesis of gastritis to cancer on the basis that the residual lesions resulting from incomplete repair of the gastric mucosa are (a) accumulations of lymphocytes, (b) thickening and disorganization of the muscularis mucosa, (c) effacement of the specialized peptic and acid cells of the mucosa and (d) hyperplasia of the fundamental or mucous cell of the mucosa (These findings are particularly true in atrophic gastritis.) Now, so long as the peptic and acid cells are still present, the phenomena of organized repair can take place in a regular cycle. But, should destruction of these specialized cells be present, disorganization of reparative processes results to such a degree that independent and disorganized proliferation of cells can produce a cancer The REVIEWERS have quoted Robertson in many places, verbatim, because of the great significance of these observations The Reviewers have reiterated their belief in this old concept of Carswell and Matthieu 100 years ago and 50 years ago, respectively, and it is extremely interesting to find such a striking course of events portrayed so brilliantly by Robertson.

B. B. Kirklin¹¹ presents the radiologic opinion of the Mayo Clinic and concludes: (1) Negative roentgenologic findings do not rule out the presence of gastritis despite marked changes. (The Reviewers expressed this view in a communication 4 years ago.) (2) A small percentage alone of gastritis is diagnosable radiologically.

G. E. Eusterman from clinical aspects discusses the symposium and expresses the opinion that "it is apparent that ulcers, polyps, adenomas and chronic gastritis are the precursors of carcinoma."

The authors reviewed some of their work during the past 5 years and further discuss their old belief that gastritis is one of the forerunners of cancer of the stomach.²³ They further draw attention to a finding which they have observed, viz., that the hypertrophic and nonanemic atrophic form of gastritis are the ones which do not appear to improve objectively (through the gastroscope) These authors further discuss the nervous element as an etiologic factor in the development of chronic gastritis They describe the nervous symptoms in gastritis, and compare the local gastric changes, on a psychogenic basis, to other gastrointestinal diseases which are known to have some etiologic basis in the disorganized psyche, such as peptic ulcer, "anorexia nervosa," etc. These authors further comment on the fact that patients with chronic gastritis may have tenderness or pain to palpation over the area corresponding to the x-ray gastric silhouette

Treatment — In the treatment of chronic gastritis, the only new addition to the therapeutic armamentarium is that put forward by M B Kunstler.¹² This author claims that gastric lavage with colloidal solutions of aluminum hy-

droxide is "curative" in chronic gastritis. Kunstler uses "Creamalin" in the dilution of 2 tablespoonfuls to the quart of warm water. A pint of the solution is used at a time and permitted to drain back by syphonage, repeating the process 3 or 4 times after which time a clear wash is generally obtained. The lavage is given once or twice daily and continued for 2 or 3 weeks A constant drip may also be used, though it is very annoying

L. M. Morrison, Win A Swalm and C L. Jackson report a series of cases in which a nonulcerous cause of the peptic ulcer syndrome was found after thorough and exhaustive studies.

Gulzon and Apendulis9 carried out an experimental study on the effects of intra-abdominal circulatory stasis on the stomach in 12 dogs with gastric fistulas They compressed the portal vein, since complete portal vein ligation caused death in from 2 to 5 hours Gastroscopy through the fistula showed the picture of venous stasis with reddening of the mucosa, edema, a marked appearance of erosive - hemorrhagic - fibrotic gastritis This persisted for some time and then progressed to hypertrophy Histologic studies were carried out at this stage and gave a significant and characteristic picture of gastritis. This was checked by

gastroscopic and histologic studies on control animals without gastric fistula. It required from 8 to 14 days after the application of stasis to establish the gastritis. Gulzon and Apendulis further studied the histamine elevation in the blood following these procedures and expressed the opinion that a toxic, "hematogenous" gastritis arises from this stasis, as evidenced by the elevation of the blood histamine level and related substances

Dobreff⁷ reports the use of *insulin* to produce an acceleration of the process of digestion in the stomach of cases with ulcer and gastritis. No statement is made of the method of diagnosis of gastritis but Dobreff claims in a series of 25 cases, 18 "cures" and 5 improved. The dosage of insulin used was 10 units in the morning, 15 units at noon and 20 units in the evening

Mahle¹⁷ reports the use of a polarigraphic technic of studying the gastric secretions in the diagnosis of gastritis. Various charts are recorded and this author claims that it is possible to diagnose gastritis by this elaborate and indirect method and that even differentiation is possible, of an atrophic gastritis due to primary pernicious anemia and an atrophic gastritis due to cancer of the stomach

GALL-BLADDER DISEASE

By J Warren Hundley, MD.

Physiology—In a review of the recent subject matter on biliary-tract disorders, Greene and Hotz²⁶ refer to the data accumulated by Carter, Greene, et al.,²⁷ on the etiology of gall-stone formation. Since the time of Naunyn, a mass of clinical and experimental data dealing with gall-stone formation has

been accumulated, and a multitude of theories have been propounded to explain the causation of gall-stones. Carter, Greene and their co-workers have emphasized again the multiplicity and complexity of the factors which apparently enter into the formation of biliary calculi. In addition, there are several varieties of gall-stones. These authors have suggested that while the factors affecting the formation of gall-stones are multiple, they may be divided into 2 groups. The first group is related to change in the hepatic bile, while the second is related to changes taking place directly in the gall-bladder or bile ducts. These investigators have reported on a series of 239 cases, with complete preoperative and postoperative studies, and have investigated the applicability of the various theories in explaining the origin of the stones.

They have pointed out that their study served to emphasize the difficulty of determining the causation and pathogenesis of gall-stones solely by study of the patient at the time of operation If the deposition of a calculus depends on the concomitant action of several different factors, then the period of calculous formation may be limited in extent, and a study of the patient 1 to 25 years later will fail to present the true picture of the conditions determining the deposition of the stone. It must also be recognized that the different types of gall-stones may differ as to causation. When the various theoretical factors advanced as possible causes of gall-stones were studied, these authors found no single factor or combination of factors which satisfactorily explained the origin of biliary calculi. In their series of cases, stasis was the only 1 of the factors considered that could be demonstrated in 25 per cent of the cases of gall-stones They consider the presumptive evidence that stasis is of importance in the formation of gall-stones, but have pointed out that other unknown factors must also be in operation, for stasis was found in the majority of noncalculous gall-bladders as well.

Schube, Myerson and Lambert, 28 in a study of the effect of benzedrine,

benzedrine and atropine and atropine alone on the gall-bladder, found that, except in the odd case, benzedrine delays the emptying of the gall-bladder only after a long period has elapsed following administration of the drug; and that sympathetic stimulation, if it is effective. occurs only after a prolonged period. It would appear that the combination of a sympathetic stimulant and parasympathetic paralysant is effective in delaying the gall-bladder emptying, but that this effect is not so marked as when the parasympathetic paralysant, atropine, is used It cannot definitely be stated whether these results are due to direct or to indirect action of the drug on the gallbladder. It seems, however, that although the results obtained by the use of benzedrine are questionably sympathetic, those obtained by use of atropine are definitely due to parasympathetic This would indicate that paralysis. should a drug be desired to relax the gall-bladder, a parasympathetic paralysant would be of greater value than a sympathetic stimulant. The authors conclude the immediate effects of benzedrine on the gall-bladder are negligible; benzedrine and atropine combined definitely delay the emptying of the gall-bladder but not as adequately as atropine alone

These same investigators²⁹ studied the effect of acetyl-beta-methylcholine chloride (mecholyl) on gall-bladder emptying and found that in no instance did the gall-bladder empty following the administration of this drug. In addition to this, mecholyl apparently delayed the emptying of the gall-bladder after a fat meal. This delay was definite and observed in a sufficient number of cases to eliminate chance occurrence In control studies performed upon the same patients no such delay was observed. Such an observation can mean only one thing, i e, that mecholyl in addition to acting as a para-

sympathetic stimulant on the gall-bladder per se also sets in motion another series of events which makes the gall-bladder incapable of emptying after the administration of a fat meal. The actual mechanisms producing such inhibition are at present unknown.

In an effort to determine the course of gall-bladder disease before the age of 30 years and the end results following cholecystectomy, Bearse³⁰ analyzed a series of 63 cases operated upon during the first 3 decades of life; 63 patients operated on for disease of the gall-bladder before the age of 30 represented 21 per cent of 300 consecutive cholecystectomies. Operation before the age of 30 does not mean that the disease is necessarily of short duration, 5 patients (7.9 per cent) had symptoms for 5 or more years and 1 had symptoms for 12 years

Only 4 patients (63 per cent) had acute cholecystitis and 59 patients (93 6 per cent) had chronic cholecystitis. Gallstones were present in 41 cases (65 per cent), this included 3 of acute cholecystitis

Three patients had stones in the common duct, an incidence of 4.7 per cent, but when the incidence was based on the 41 cases of calculous gall-bladder it was 7.3 per cent. The duration of the symptoms in these cases varied from 4 to 7 years.

Fifty-seven patients (904 per cent) were followed after operation, 53 (929 per cent) were free from symptoms when last seen. Thirty-six patients (972 per cent) of 37 with cholelithiasis were entirely relieved, 17 of 20 with noncalculous chronic cholecystitis (85 per cent) were either greatly improved or completely relieved.

M. Feldman,³¹ in a comparative study of the single- and double-dose methods of dye administration for cholecystography, reports 200 cases so studied, one-half of

which were given a large single dose of the dve and to the other half the dve was administered in 2 doses. By the single dose method, a minimum of 6 grams of tetraiodophenolphthalein was given to patients weighing up to 160 pounds (72.7) kg.); 9 grams to patients weighing up to 160 to 200 pounds (72.7 to 909 kg.) and 12 grams to patients weighing over 200 pounds With the double dose technic, 3 grams of the dye was administered at noon, and 3 grams at 6 P. M. An additional dose of dye was given at 9 P M. to those weighing over 175 pounds (80 kg) in order to equalize the dosage factor in the 2 series.

On the basis of this study, Feldman arrived at the following conclusions:

- 1. The diagnostic results following the administration of a large single dose of tetra-iodophenolphthalein in cholecystographic studies of the gall-bladder do not differ in any way from those of the double-dose method
- 2 The single-dose method simplifies the cholecystographic test. The dye is given by the technician or roentgenologist, making certain that the full amount is administered at a definite time.
- 3 The double-dose method offers no superior shadows over those obtained by the single-dose procedure.
- 4 The double-dose method does not prevent or lessen the reactions of the dye upon the digestive tract
- 5 The prolonged period of absorption of the dye from the intestine is theoretically of some advantage, but is not necessary, except in cases of extreme diarrhea, for the production of normal vesicular shadows
- o Regardless of whether the single-dose or the double-dose method is utilized, good results may be secured by either procedure, providing a sufficient amount of the dye is administered.

Treatment—Recent contributions to the subject of the treatment of chronic gall-bladder disease, indicate very definitely that the trend is more and more toward the more conservative management, particularly of chronic cholecystitis without stones. The degree and likelihood of symptomatic relief by *cholecystectomy* is apparently more dependent on the presence of stones or a history of attacks of true gall-bladder colic than on the pathologic state of the gall-bladder.

It is in the noncalculous group of cholecystitis that cholecystectomy has been disappointing. As all available reports of surgical experience show, the major factor which determines the success or failure of cholecystectomy is the presence or absence of biliary colic. If true biliary colic has been a feature of the complaint, a cure may almost be assured no matter what pathologic changes may be present in the gall-bladder, but if this feature is lacking, the probabilities of success are greatly reduced. What is to be done with the "nonoperated case" of noncalculous cholecystic disease? Snell³² feels that the usual "gall-bladder diet," low in fat and cholesterol is ineffective even when fortified with saline laxatives and antispasmodics. Duodenal drainage in the majority of instances, accomplishes little in relieving symptoms. The application of physiologic principles to treatment has only recently been undertaken and the results to date are at least encouraging. Ivy33 has recommended a diet as high in fat as the patients' tolerance will permit, together with bile salts to encourage biliary flow and the cautious use of alkaline or saline laxatives below the dosage likely to produce a "cathartic colon" Wilkinson34

advises a bland diet with frequent feedings, sedatives and antispasmodics, and Andresen³⁵ advises a somewhat similar regimen. Mock. Brown and Dolkart³⁶ advise a regimen of hourly feedings of milk and cream, the use of bile salts (ketocholanic acid), and sedatives with antispasmodics. The essential principles of all of these forms of treatment are the same; the higher intake of fat stimulates frequent contraction and emptying of the gall-bladder, the bile salts increase biliary flow and perhaps serve to relax the choledochus sphincter, and the sedatives and antispasmodics reduce the irritability of the sphincteric mechanism and the duodenum. Good results are by no means universally obtained with therapy of this type, but in cases in which the surgical indications are not clear, medical management along these lines may be recommended, at least until further observation has been carried out.

In discussing the indications for surgery in chronic cholecystitis, Elkin³⁷ feels that the gall-bladder without stones should not be subjected to operation unless the symptoms are very clear cut and definite and unless the cholecystogram shows evidence of a gall-bladder which functions improperly or not at all ln this as in other diseases, it must be remembered that relief of symptoms is in proportion to their severity and in the absence of gall-stones, other organs, particularly the stomach, duodenum and colon, should be carefully investigated before removal of the gall-bladder

PEPTIC ULCER

By Charles M. Thompson, M.D.

Etiology and Pathogenesis — The constitutional factor has been frequently pointed to as being the fundamental in ulcer causation. This broader view of

the patient rather than of the local disease is quite generally accepted. Eusterman³⁵ believes that peptic ulcer is not the result of any single agent but of an

interaction of several and that the constitutional factor is basic.

Constitutional predisposition has as its effect a tissue susceptibility or weakness upon which other factors can produce organic change. Realizing the magnitude of these numerous factors and their interactions, it can be agreed that ulcer itself is a symptom of a more general disorder. Most writers agree with Milligan³⁹ that unless the underlying factors are corrected, the results of therapy will be unsuccessful. Thus the importance of a study of the etiology of ulcer. The factors are reviewed in what seems to be the order of their importance and mention in the literature.

Neurogenic — Since Cushing showed the occurrence of peptic ulceration associated with brain lesions and the importance of influences from cerebral autonomic nerve centers, investigation of this relationship has been stimulated Eusterman³⁸ states, "emotional conflict +ulcer diathesis=ulcer", thus emphasizing the importance of the psychic element in the etiology. Disharmony between the vagus and sympathetic nervous systems produces localized spasm in the muscles of the stomach and duodenum and terminal vessels. The psychic control of such vegetative imbalance is recognized, and the rôle of the emotions can be agreed upon. This imbalance causing spasm and other unphysiologic effects leads to submuçosal ischemia and anoxemia The first organic changes in this sequence are mucosal erosions and hemorrhages, which, while acute and temporary, may become chronic and permanent if the operating factors are not removed The chronic effect is peptic ulcer

Necheles⁴⁰ carried out 3 experiments on the origin of gastritis and peptic ulcer in dogs. Injection of small amounts of acetylcholine was followed by a hemor-

rhagic condition of the upper gastrointestinal tract. Constant injection of moderate amounts of pitressin was followed by a hemorrhagic condition of the entire gastrointestinal tract. Both acetylcholine and pitressin cause vascular contraction in the stomach and duodenum. Acetylcholine is the vagus principle and is liberated by efferent impulses at the endings of the vagus in the stomach, where it constricts the blood vessels and acts as a stimulant for gastric acid secre-Afferent impulses in the vagus tion cause an outpouring of posterior pituitary principle, although the authors were unable to reproduce the hemorrhagic condition by stimulation of the right central vagus. Eusterman³⁸ includes in his neurogenic theory the importance of parasympathetic hypertonus The effects of this action are presumably worse where the most branches of the vagus occur and where most arteries are end This is true along the lesser curvature and in the duodenal bulb. Patients with ulcers have greater vagus effect (i e, imbalance) leading to spasm, hypersecretion and hypermotility. It is Necheles'40 opinion that acidity may be high or low, for little acid is needed for the digestion of a devitalized spot

In association with experimental work on nervous lesions as the fundamental cause of peptic ulcer there are clinical observations repeatedly noted in the literature Opper and Zimmerman⁴¹ demonstrated erosions in the esophagus, stomach and duodenum in 21 cases of brain lesions Gauss⁴² enumerated gastrointestinal symptoms in certain diseases of the brain. The lesions studied produced various syndromes, including peptic ulcer. Thus it has been demonstrated that peptic ulcer and erosions of the upper gastrointestinal tract occur with brain lesions There seems to be in the cortex both a motor and a sensory autonomic representation. The pathways of these are through the midbrain and ultimately the vagus. Irritation of these pathways is believed to occur in intracranial lesions; thus producing symptoms and in some cases pathological changes. These cerebral autonomic nerve centers are intimately connected with the psyche and are naturally responsive to it.

(2) Vascular—The rôle of an atherosclerotic process in the gastric vessels in gastric hemorrhage is well understood. The rôle of such a process in the causation of uncomplicated peptic ulcer is not generally accepted but its corollary, spasm of the vessels, is given increasing importance. There is a very close relationship between vasospasm and neurogenic imbalance. In fact, most experiments on the neurogenic origin of ulcer begin or end with the premise of vasoconstriction, ischemia and tissue death. Boles, et al.,43 studied 161 cases which at postmortem showed acute focal lesions of the gastric mucosa. These lesions were in the nature of focal necroses, ulcerations and desquamations of the acute type in the mucosal layers and a more chronic process in the deeper lav-The investigators concluded that ers focal gastric lesions of this type were due to a chronic circulatory insufficiency which affected the stomach more intensely due to its vascular peculiarities and its rich vasomotor innervation. They showed that this resulted from (1) cardiovascular disease. (2) metabolic disturbance. (3) primary cerebral disease or vasomotor disturbance, (4) secondary anemia and chronic infection. is theorized that these factors acting singly or together produced a qualitative or quantitative circulatory insufficiency which encouraged the breakdown of tissue This theory is compatible with the idea of neurogenic origin. In both there is suggested an alteration in the viability

and health of tissue, the modality of which remains to be discovered. Wilhelmj states that these acute focal lesions become the chronic ulcer only after repeated insults.

- (3)Acid - erosion — Eusterman³⁸ states that gastric hypersecretion is an important factor in the genesis of ulcer. No doubt this factor is dependent for its action on the factor of tissue defense, which in turn is affected by some deeper change in the organism as shown by the experiments of Necheles, et al.40 Acid chyme digests gastric tissue when tissue resistance is lowered. Hollander⁴⁴ mentions 6 factors affecting gastric secretion. vis., (1) admixture of saliva, (2) regurgitation of intestinal contents, (3) peptic secretion, (4) secretion of a specific dilution factor, (5) mucous secretion, (6) readsorption of hydrochloric acid. All must be considered in evaluating gastric secretory mechanism. Acid digests the mucosa where tissue injury has occurred and where it is uncontrolled by neutralization, dilution, inhibition or buffering action. Most ulcers occur in the pathway of acid chyme. 45 A breakdown of tissue defense factors or an intrinsic tissue susceptibility are the beginning of injury from high acid-pepsin values. There is evidence that high acid-pepsin values alone do not cause pathology in the presence of a normal protective mechanism.
- (4) Trauma—Trauma may be external or internal. According to Kellogg, et al, 46 internal trauma may result from coarse, irritating foods; phytobezoar; or traction and compression as occur in esophageal hiatus hernias External trauma occurs in direct blows on the stomach The relation of external traumatism is discussed rather completely Most traumatic ulcers of this type are located on the lesser curvature or posterior wall of the stomach. Symptoms of acute ulceration may follow a quies-

cent period after the first shock and hemorrhage. In some cases the picture of chronic ulceration follows, Cases are cited where the full clinical picture of chronic peptic ulcer develops after variable periods of freedom from symptoms. It is believed in these cases that acid chyme acts on injured tissue.

- (5) Infection—The findings of Billings and Rosenow about 25 years ago still have a place in the study of peptic ulceration Focal infection is placed in a position of importance by most investigators Localized infection by streptococci which have a special affinity for the mucous membrane of the stomach and duodenum may be demonstrated.38 is important to observe the aggravation of symptoms in some cases from the presence of the by-products of focal disease. The interesting phenomenon of seasonal recurrence of ulcer symptoms and even hemorrhage in the fall and spring may have some relation to respiratory infection at those times
- (6) Gastritis—The theory that gastritis always precedes the development of ulcer and that ulcers never develop in a healthy mucosa has been postulated for many years without adequate substantiation. The work of Schindler, et al,47 is removing the guesswork from this theory and giving it a clearer interpretation Schindler⁴⁷ has demonstrated with the gastroscope acute hemorrhagic erosions, mucosal hemorrhages, and pigment spots (gastric purpura) in cases of gastritis of varying degree and stage He believes that these changes may have something to do with the origin of ulcer, and that hemorrhagic erosions may be the acute stage of chronic ulcer. However, Schindler and Templeton⁴⁸ could not demonstrate gastritis in a number of cases of gastroduodenal ulceration. Although all cases of ulcer do not show gastritis, the majority do. This is espe-

cially true in the more active ulceration when the surrounding mucosa is frequently swollen, red, and edematous. The rôle of gastritis in the modification of gastric physiology and the possible development of ulcerative processes is receiving increasing attention.³⁸

(7) Endocrine — This theory of the etiology of ulcer is still in the experimental stage. Recent investigators have established the importance of the posterior lobe of the pituitary gland in relation to alimentary blood flow and secre-Sandweiss, et al, 49 following a preliminary report on the prevention and healing of ulcers in dogs with anterior pituitary-like hormone (antuitrin-S) further state that the improvement in ulcer symptoms during pregnancy may be due to the large amounts of A.P L hormone in the body at that time. They review 70,310 consecutive hospital admissions for obstetrical care, and show only 1 case of active peptic ulcer a series of 46 women with proved peptic ulcer, 25 had one or more pregnancies. Of 52 pregnancies in this group, only 1 had active ulcer symptoms during pregnancy It is concluded from these statistics that ulcer is rare during pregnancy and that pregnancy has a beneficial effect on ulcer The authors suggest that there is some rhythmic interplay in the menstrual cycle between the ovaries and pituitary gland which protects the fe-Before puberty the incidence of ulcer in male and female is almost equal, while after puberty the proportion of males to females is about 4.5 to 1 symptoms of ulcer in the female were aggravated during the menopause and in women with ulcers there was a high degree of endocrine disturbance (46 per cent). Studying the effect of antuitrin-S injections on 18 patients with active ulcer symptoms, 11 became symptomfree, 3 were moderately improved and 4

were unimproved. The authors point out that this is no better than would be expected by other parenteral methods. It was also found that antuitrin-S in 1 to 5 cc. doses over long periods had no effect on the gastric acidity in dogs. However, 10 to 20 cc. injections did decrease the acid output of 2 gastricpouche dogs. Daily doses of 2 to 5 cc. of antuitrin-S for 10 consecutive days had no effect on acidity in humans.49 Other investigators 50 found no constant effect on the volume or acidity of gastric juice by the subcutaneous injection of antuitrin-S. This follows the work of Schiff, et al., in 1938 showing that estrogen had no effect on gastric acidity. This unsettled but very important question of endocrine effect is being further studied.

(8) Vitamin Deficiency — The consensus of opinion seems to be that although vitamins are important to the patient under treatment, it is doubtful whether they play a major etiological rôle ⁵¹ Vitamin A deficiency produces minute ulcerations in the stomach of the rat but this is not considered an important cause in man There is little evidence that lack of vitamin B leads to ulcer. The usual result of such a lack is atrophy and achlorhydria. The most common manifestations of vitamin C deficiency are gingivitis and hemorrhage from the alimentary tract Patients with ulcer and especially bleeding ulcers show a relatively low level of vitamin C in the blood This does not prove its causative nature, probably being only an effect of a commonly deficient diet. There is no evidence of other deficiencies in the etiology of peptic ulcer The relation of an anti-gizzard-erosion factor seen in chicks has not been shown to be of importance ın man.⁵¹

(9) Allergy—The rôle of allergy is highly debatable. That ulcer is an aller-

gic phenomenon has not been proved, but persistence of symptoms in allergic ulcerbearing individuals may occur from ingestion of allergens in the diet. Ehrenfeld, et al.,52 studied a group of 72 known allergic patients. Of this group, 35 (49 per cent) had symptoms such as gas, belching, epigastric pain, heartburn, nausea, vomiting, constipation, and diarrhea. Of the whole group, 60, or 83 per cent, had negative x-ray findings. Of the 12 with positive findings, 4 had definite duodenal ulcers and 8 suffered from spasm. A second group (75) with proved ulcers was studied. Eight, or slightly above 10 per cent, were found to be allergic These figures of the incidence of ulcer in allergic patients and of allergy in ulcer patients are well within the incidence for the general population. It is concluded by the authors that allergy is not an important etiological factor in a significant proportion of peptic ulcer patients and that peptic ulcer is not of increased frequency in the allergic group

Diagnosis-Studies of gastric secretions are recognized to be of value in the diagnosis of pepticulcer. Upham, et al.,53 state that although the various test meals in vogue are adequate for practical purposes, they have limitations, Test meals using food (shredded wheat, bread, water, tea, etc) are weak in their secretogogue effect, thus rendering them incomplete tests of the acid secreting power of the stomach Histamine is abnormal in its action The alcohol test meal acts as an irritant. These authors studied the results of the secretogogue meal developed by Wilhelmi as a gastric analysis procedure in humans.

The meal was made up in a 2 per cent solution as follows (1) Forty grams of Liebigs extract are dissolved in 1 liter of distilled water (2) Add 30 mg of the sodium salt of phenol red dissolved in 33 cc of 1/10 N NaOH (3) Add 20 cc. of a 20 per cent solution of sodium carbonate. (4) Add slowly

with constant stirring 1 liter of 1/10 N HCl. The solution is now acid to litmus paper. (5) Allow to stand until a heavy flocculent precipitate settles out. (6) Filter until crystal clear.

They⁵³ plotted various types of curves with this method. The normal curve showed a sharp rise in acid secretion in the early part of the experiment and a fairly sharp fall during the latter part. Duodenal ulcer with pyloric obstruction gave a very sharp rise in acid in the first hour with a gradual tapering off in the acid curve and a greater number of specimens. Duodenal ulcer without obstruction gave a very sharp rise in the first hour and almost as sharp a drop in the second hour. They state that although this test meal is still in the character of a laboratory procedure, it gives more information as to the actual amount of HCl produced by the stomach, as well as the amount of non-acid and acid fluid added to the gastric contents by the stomach wall and by duodenal regurgitation. They believe that with the ordinary Ewald cracker meal, there is a binding of hydrochloric acid by the meal in the first hour which confuses and makes unreliable the acid values.

Wilhelmi, et al ⁵⁴ state that when this test meal is used, it is possible to determine the following factors on each gastric sample: (1) What proportion of the sample is fluid of the test meal still remaining in the stomach and what proportion are secretions which have entered the stomach. (2) The total secretions entering the stomach can be separated into acid and non-acid secretions (3) The acidity of the total secretions entering the stomach can be determined independently of the mixed gastric contents. After introduction of the test meal, samples (35 cc.) were taken every 15 minutes until no further contents could be obtained. These authors argue that when the Ewald procedure is used, the curves

are terminated at an arbitrary period (1 hour), and that this may fail to show the peak of the response in patients with a long, slowly developing curve.

The differentiation between benign and malignant gastric ulceration is a matter of careful diagnostic study. Finsterer⁵⁵ reports a statistical study on 141 cases of malignant ulcer that came to operation. In this series there was only 9.3 per cent of cures. He believes that the criteria for distinguishing early signs of malignant degeneration are so untrustworthy, that all cases of gastric ulcer should be resected. Milligan³⁹ describes 3 criteria which he considers of value, viz, (1) at the end of 1 month of accurate management the ulcer defect must have disappeared or be considerably smaller, (2) at the end of the same period the subjective symptoms must be relieved, (3) at the end of the same period the benzidine test must show an absence of occult blood. If the treatment succeeds in doing all of these things, the patient is advised to continue medical management under close observation. The opposite result indicates surgical interference. Allison⁵⁶ states that benign gastric ulcers usually occur in the ulcerbearing area, ie, from the cardia to the pylorus on the lesser curvature, extending only a short distance over the anterior and posterior walls. Malignant ulcers may occur in any portion of the stomach He advises a 3 weeks' treatment with the Sippy program to differentiate. Friedell⁵⁷ agrees that the criteria for differentiation are fallible and advises that when the slightest doubt is present. the patient should have the benefit of surgery. He states that the possibility of an ulcer of the stomach being malignant must be considered in any age group. He shows that, although not common, carcinoma of the stomach may occur during the third decade. According to this author, the tendency for a small gastric lesion to be benign is especially true when the patient is less than 30 years old; when the symptoms are of the ulcer type; and when the concentration of free HCl is greater than 60 clinical units. It becomes less true as the age of the patient increases; the duration of symptoms and the concentration of free HCl decreases; and when the history is of the non-ulcer type. He recognizes only 3 criteria. The meniscus sign of the roentgenologist and a lesion of greater diameter than that of a silver dollar point to malignancy. Permanent healing by medical treatment proves the lesion to be benign.

Pfahler⁵⁸ points to the more accurate methods of x-ray diagnosis used by present day roentgenologists. Mucous membrane relief studies, using thin mixtures of barium given in small doses, give a more detailed study of the mucosal pattern of the stomach. Early peptic ulceration as well as certain stages of gastritis and early carcinoma are most adaptable to diagnosis by this method. Mucous membrane relief studies of the duodenum, with compression over the area. are useful in detecting early changes from duodentis to superficial ulceration. The author considers this method an advance over the method using heavier mixtures of barium in larger quantities, when the diagnosis involves the earliest type of gastroduodenal pathology. Templeton and Schindler⁴⁸ state that in some cases the filled stomach shows the ulcer better and that the latter method should always accompany the relief method of study

Gastroscopic examination is an adjunct to the roentgenologic examination. Schindler⁴⁷ states that gastroscopy and x-ray study are 2 methods aiming at the same goal, vis, an accurate anatomic diagnosis. This author does not believe

that x-ray relief pictures demonstrate changes in the gastric mucosa as well as the gastroscope. He believes that a combination of both methods gives the best results. He agrees that in the diagnosis of chronic gastroduodenal ulcer careful x-ray compression relief technic is superior to gastroscopy. Duodenal ulcers are not accessible to the gastroscope and pyloric ulcers are often not visualized due to adhesions and dislocation of the area. Blind areas in the path of the scope may hide lesions. Schindler⁴⁷ further argues that the differential diagnosis between benign and malignant ulcers is an important part of gastroscopy and that every patient over 35 years of age in whom a gastric ulcer niche has been demonstrated by x-rays, should be gastroscoped. Templeton and Schindler⁴⁸ correlated the roentgenologic and gastroscopic findings in a number of cases. Of 41 cases of gastric ulcer, 33 were seen equally well by the x-rays and gastroscope. Seven were seen by the x-rays but not by the gastroscope; 4 were seen by the gastroscope but not by x-rays. Of the 7 seen only by x-rays, inaccessible areas in the antrum and near the esophageal orifice were responsible for 5; 2 others were on the lesser curvature and presumably covered by mucosal folds. Of the 4 seen only by the gastroscope, 2 were shallow lesions and 2 were high on the posterior wall. Freeman⁵⁹ states that, although the greatest field of usefulness for the gastroscope is in the differentiation of chronic gastritis from functional disorders, it has an important usefulness in: (1) The diagnosis of gastric ulcer, (2) its differentiation from malignant ulcer, and (3) cases of recent hemorrhage where the history and all other available studies leave the cause obscure. A superficial gastric ulcer may be diagnosed gastroscopically when the diagnosis is not possible from x-rays

Two interesting phenomena of hemorrhage from peptic ulcer have diagnostic connotations It has been noted that patients who have lost large quantities of blood will often show elevated blood urea values. Crohn, et al,60 believe that the increased value for blood urea during hemorrhage is an index of the degree of circulatory collapse. These authors feel, however, that blood pressure estimates rather than blood urea determinations constitute a better, simpler, and quicker guide to the extent of shock and failure. Schiff, et al, 61 showed that the intragastric or intrajejunal administration in man of single doses of 250 to 1000 cc. of citrated blood is followed by a significant rise in blood urea nitrogen The increase was proportionate to the amount of blood administered. It also depended on the portion of the tract into which the blood was placed, occurring earlier and to a greater degree when the blood was introduced into the stomach than when it was introduced into the jejunum or upper ileum They concluded that the increase of blood urea nitrogen following the introduction of blood was due to the digestion and absorption of blood Dill, et al.,62 noted that the incidence of fever was 53 per cent in a series of peptic ulcer cases drawn from hospital records. The incidence of fever in bleeding peptic ulcers was 80 per cent and 46 per cent of nonbleeding ulcers were febrile. These authors conclude that there is no significant causative factor for this; but that large hemorrhage, anemia, and a labile vegetative nervous system are probably important in the production of fever

Treatment—Diet—The hourly Sippy program for the initial treatment of the uncomplicated ulcer is the choice of most authorities. Nicol⁶³ considers the feeding at 2-hour intervals of a mechanically non-irritating type of food containing more protein superior to the hourly plan

of Sippy. This author considers physiological and psychological rest more important than diet. The 2-hour interval between feedings is favored by others who consider it more efficacious in healing.39 Windwer, et al,64 found that in 40 patients, 90 per cent were symptomatically improved on a high protein diet of the bland type, containing 150 Gm. of protein, 100 Gm. of fat, and 200 Gm. of carbohydrate. The proteins were given in the form of lean boiled meat, chicken, cottage cheese, milk, and unflavored gelatin. The important place of vitamins in the treatment of the patient is reviewed Experimental work on vitamin C levels and requirements is being reported Warren, et al, 65 state that patients with active peptic ulcer utilize more ascorbic acid than do normal individuals and that the ordinary ulcer diet is deficient in this factor They advise giving the juice of 1 or 2 good sized oranges, or crystalline ascorbic acid in doses from $1\frac{1}{4}$ to 3 grains (75 to 200 mg) daily. These authors state that there is no present evidence that vitamin C has any direct healing effect on ulcer However, with low plasma values and a diet known to be deficient, there is ample basis for feeding the patient vitamin C in one form or other

Alkalis—A more critical estimate of what alkalis accomplish has been made Systemic alkalosis, gastric irritation and rebound hypersecretion of acid, renal calculosis and nutritional interference have all been the dangers of too arduous alkaline therapy. There is a difference of opinion as to the value of complete neutralization and whether alkalis accomplish this ideal. 63, 66, 67 It has been suggested that the importance of free acid in the stomach in interfering with the healing of ulcers is over-emphasized 63 Adams 68 states that even though healing does take place in the presence of acid

activity, recovery would be facilitated by the practical absence of free acid. Antacids are used to allay pain; to relieve pylorospasm; to protect the lesion from the action of acid chyme. Whether the antacid used accomplishes these purposes without harmful side-action depends on a careful individualization of the treatment.

Systemic Alkalis — These are (a) Sippy powders, sodium bicarbonate, sodium and potassium citrates, and acetates. They have good neutralizing powers. Their action is rapid, short-lived, and, when given in large continued dosages, they may cause systemic alkalosis, especially where renal impairment or pyloric obstruction are present 68 Their second disadvantage is that they cause a rebound secretion of acid which is greater than before neutralization was attempted Although most cases resulting in alkalosis had a pre-existing degree of renal impairment, cases have been reported where the normal kidney may suffer from long continued use of systemic alkalis 68 Eisele⁶⁷ advises in doubtful cases a study of the patient's renal function by either the concentration test or urea clearance test before using the absorbable antacids. The question of renal calculi resulting from long continued use of alkalis has been studied by Kretschmer, et al 69 Six hundred and eight ulcer cases treated with milk and alkalis are reported, and in this group there was a difference of only 18 per cent in the incidence of stone formation after the use of alkalis. In a group of 1260 kidney and ureteral stone cases there was only an incidence of 12 per cent for those who had previous ulcer treatment of this type. The authors concluded that the differential is too low to indict alkalı as a cause of calculi

(b) Non-systemic Alkalis—These are the antacids, either soluble or insoluble, which are practically unabsorbed from

the alimentary canal. They do not cause alkalosis. They are assuming a more important position in the therapy of ulcer. Adams⁶⁸ evaluates the most commonly used non-systemic antacids. Magnesium salts, including the oxide and carbonate, have the disadvantage of causing a rebound secretion of acid and they are irritating to the intestines. Magnesium oxide has good neutralizing properties and it is combined advantageously with other less irritating antacids. Tribasic magnesium and calcium phosphate shows good neutralization and is less apt to cause an acid-base disturbance 70 Magnesium trisicilate gave a slower but more prolonged reduction of acid than the systemic antacids. It has great neutralizing powers, it is not absorbed; it has the advantage of prolonged action; and it had no effect on the bowels according to this author 71 The advantage of prolonged but delayed action makes it particularly applicable to cases with night pain and hypersecretion. Calcium carbonate39 is a non-systemic alkali which does not provoke a secondary secretion of acid. It protects and has demulcent properties, but it is also capable of causing constipation and fecaliths. Milligan, 39 outlining an ambulatory treatment, alternates a No 1 powder (calcium carbonate, 30 grains-2 Gm) with a No 2 powder (calcium carbonate, 10 grains—06 Gm, magnesium oxide, 10 grams—06 Gm) every 2 hours during the day until 7 P M, and then every half hour until 9 P M. He states that there is no danger of alkalosis on this plan Mucin has demulcent qualities but its value as an antacid is very limited 65 The preparations of mucin are expensive. Brown, et al.,66 report the use of 4 daily doses of mucin totaling 1 to 2 drains (4 to 8 Gm.) in conjunction with frequent feedings and antispasmodics in reducing the incidence of recurrences,

Vegetable mucilage has a place in relieving the symptoms of irritable bowel seen commonly in ulcer patients. Bismuth is protective and demulcent but is relatively ineffectual as a buffering agent. 68

The most important work on nonsystemic alkalis has been done on colloidal aluminum hydroxide. It has a high buffering action and is amphoteric. It is highly adsorbent, is easily administered, and may be used by the drip method.⁷² Adams⁶⁸ states that it combats 3 things in ulcer: (1) Trauma by its protective action; (2) acid corrosion by its antacid action, and (3) infection by its adsorbent action. Colloidal aluminum hydroxide may be given in large doses without danger of alkalosis. It is an important agent in cases of hypersecretion and in cases which do not respond to other medication

This method is well adapted to prolonged use in cases that are slow to respond and so far has been effective in controlling recurrences 72 Aluminum hydroxide is effective in relieving the pain in severe cases and, according to Kyger, et al, in controlling hemorrhage 72 Rutherford, et al.,73 state that use of colloidal aluminum hydroxide is indicated in (1) Cases of peptic ulcer of a severe type and with marked hypersecretion, (2) cases which have not responded to other types of therapy, (3) cases with postoperative jejunal ulcer which have not responded. and (4) cases of peptic ulcer associated with renal impairment. These authors use the drip method in cases with marked hypersecretion and night pain Using a mixture of colloidal aluminum hydroxide (1 part) and water (3 parts), they regulate it to about 15 drops a minute addition, 90 cc of milk and cream are given every hour.

Such an apparently ideal method should have some flaws in it. Constipation is an occasional result, especially in bed

patients. This is usually easily controlled and is not so common in ambulatory patients.68 Rectal palpation is a necessary examination in bed patients who are taking the preparation for long periods. Quigley, et al.,74 administered massive doses to dogs for 79 days. No significant effect on gastric emptying time was demonstrated. The secretory response to histamine was only temporarily reduced. Other investigators 75 gave variable doses of colloidal aluminum hydroxide to dogs, in attempting to prevent postoperative jejunal ulcers. Neither in small or large doses did the preparation have any value When doses large enough to control free acid were given continuously, there was a decrease in appetite. a decrease in dietary intake, and a more rapid loss of weight.

Antispasmodics - Belladonna and its alkaloid, atropine, are used generally for their antispasmodic action in peptic ulcer Recent work on a synthetic preparation is reported. Necheles, et al.,76 studied the effects of a new spasmolytic drug, diphenylacetyldiethylaminoethanolhydrochloride (trasentin), on the rat and the dog They found that the drug diminished or abolished spasm and contraction of the stomach, small and large intestine, produced by various drugs or vagus stimulation in anesthetized dogs. They further state that the relaxing effect was due to 2 mechanisms: (1) That which acts on the muscle directly (papaverine-like effect), and (2) that which acts on its parasympathetic nerves (atropine-like effect) A later report⁷⁷ reviewed the effect of the drug on 12 patients with gastric or duodenal ulcer. As a group, the beneficial effects were no greater than in the usual forms of therapy. However, trasentin produced relief or improvement in a number of cases in which the other measures were not of much help. The optimal dose by mouth

was found to be 150 mg. (2 pills each of 75 mg.) usually given 30 minutes before meals; by subcutaneous injection, 75 mg. (1 ampoule). They conclude that *Trasentin* is of value and has a place among the effective antispasmodic drugs.

Hormone Therapy—The use of hormones in the treatment of ulcer is receiving some degree of publicity. Metz, et al.,78 reported that 24 out of 28 patients had symptomatic relief after the use of a fresh preparation of the posterior lobe of the pituitary administered orally. hypodermically, or by the intranasal route. The latter method was preferred and gave the best results. It is still too early to comment on this. The effect of anterior pituitary-like hormone has been studied by Felson,50 Sandweiss, et al.49 These authors found no constant effect on the volume or acidity of gastric juice from the subcutaneous injection of antuitrin-S. Sandweiss, et al,49 gave 200 to 500 rat units of antuitrin-S to 18 patients with active peptic ulcer symptoms, daily for 14 consecutive days. These patients continued the customary dietary régime but received no alkalis or antispasmodics. Although 11 of these patients became symptom-free and 3 were moderately improved, the authors stated that the results were not unlike those from other parenteral methods Relating the apparent beneficial effects of pregnancy on ulcer when the body is literally flooded with A P. L. hormone to the dosages used in their experiment, they are unable to state at this time whether higher dosages of a more concentrated solution will give better clinical results.

Treatment of Hemorrhage—Blackford, et al, ⁴⁶ showed in a certain group that 96 per cent of the deaths from hemorrhage were in patients over 45; the remaining 4 per cent being in patients under 45. They argue that operation in the younger group is not usually indicated

in the absence of other complications. They further state that massive hemorrhage from ulcer in patients over 45 should be treated early by surgical interference. Brown, et al.,47 state that the group in the latter decades of life with sclerotic vessels and in whom rapid exsanguination takes place should be treated by surgery, instituted at the proper time. Allen, et al.,48 conclude that (1) 1 massive hemorrhage is an indication for operation in the patient over 50, (2) a single hemorrhage in the younger patient demands a careful medical regimen, but if ulcer symptoms or a second hemorrhage occurs, surgery is indicated, (3) when operation is decided upon it should not be delayed more than 48 hours. Crohn²⁶ prefers the medical expectancy of 9.1 per cent of deaths in the advanced age group who bleed, to the risks and necessary fatalities which may reasonably be expected by a radical surgical approach. Andresen⁵⁰ outlines a complete medical program but relegates surgery to a last choice.

Andresen, 50 following the lead of Meulengracht abroad, feeds his hemorrhage cases early. His program is (1) absolute rest and morphinization for the first 24 hours, (2) feedings immediately after the hemorrhage, using a gelatin-milk mixture consisting of gelatin, 30 Gm.; dextrose, 60 Gm; cream (20 per cent), 100 cc; milk, 900 cc. Six ounces of this mixture are given every 2 hours for the first 4 days On the fifth and sixth days he adds to 4 of these feedings either 1 egg, 3 oz. of cereal, custard, jello, or ice cream. On the seventh and eighth days he adds two of the above foods to each of 3 feedings. On the ninth day he starts his regular liberal ulcer diet.

Turnbull and Sage⁵² report a mortality of 2.5 per cent. Mayer, *et al*, ⁷⁹ treated a total of 74 cases with 4 deaths. They used a method similar to Meulengrachts'.

Using alkalis they gave a puree diet consisting of:

6:00 A. M.—Tea, white bread, and butter.

9:00 A. M.—Oatmeal with milk, bread and butter.

1:00 P M —Dinner including a variety of dishes as meat balls, broiled chops, omelette, fish balls, vegetable purees, vegetable soups, gruel, stewed apricots, apple sauce, rice, and tapioca pudding. The patients are allowed to eat as much as they want.

3 00 Р м -- Сосоа.

6:00 P M —White bread and butter, sliced meats, cheese, and tea.

Their conclusions were: (1) The patients tolerated the diet well and were more comfortable, (2) abdominal pains were infrequent and little morphine was necessary, (3) none of the patients became irrational as in starvation therapy, and (4) pulmonary complications and parotitis were not encountered and the return of strength was more rapid Hartman⁸⁰ gives nothing by mouth for 24 to 48 hours and then initiates a Sippy diet. He stresses the importance of vitamins in the diet, especially vitamin C in potential bleeders and urges the use of this factor. Crohn⁶⁰ decries the use of the Meulengracht diet following severe hemorrhage. He advises a period of starvation and from then on a diet as liberal as possible

Andresen⁸¹ advises the withholding of transfusions whenever possible. If there is severe anoxemia or other indications,

he gives 150 to 200 cc. of blood. Crohn⁶⁰ uses transfusions sparingly if at all. His indications are anoxemia, a falling blood pressure below 90 systolic, and a hemoglobin below 35 per cent. Transfusions are preferably given after the blood pressure has been stabilized and when the symptoms of shock have subsided. LaDue82 withholds parenteral and intravenous fluids whenever possible. Other authors^{80, 83} state that transfusions can be given safely for shock, loss of blood, and nutrition They discount the danger of elevating venous or arterial pressure Browne⁸³ states that parenteral fluids should be given freely to maintain nutrition, water balance, circulating volume, and to combat acidosis

Kyger, et al.,72 have used aluminum hydroxide by the drip method in bleeding ulcer. Other authors83 state that this offers the best means for physiological control of the hemorrhage The purpose is to control acidity and peptic digestion. Absorbable alkalis are not commonly used in peptic ulcer hemorrhage Mayer, et al., 79 give 1 teaspoonful 3 times a day of a mixture consisting of sodium bicarbonate, and magnesium subcarbonate āā, ½ ounce (15 Gm), extract of hyocvamus, 2 grains (013 Gm.), with the Meulengracht plan. They give iron in the form of ferri lactas, $\frac{1}{2}$ grain (003 Gm) 3 times a day

REGIONAL ILEITIS

By R R Strawbridge, M D

In its broad concept, regional ileitis can be defined as an acute or subacute but usually a chronic nonspecific, granulomatous inflammatory process of undetermined origin which occurs for the most part in the terminal segment of the ileum but which may be found involving either the large or small intestine separated by "skip areas" of normal bowel. Clinically, it is characterized by diarrhea, fever, obstructive phenomena, and fistulous tracts and lends itself favorably to surgical intervention.

Incidence and Etiology—No one is immune but all records show it to be a disease of youth with an average age of 27.8 in Crohn's ** most recent reports with extremes of 5 and 9 to late 60 reported by Rosi and Meyer. *5 The Hebrew race is more frequently involved and the Negro apparently the least. Males slightly predominate with a ratio of about 3 to 2. There seems to be no familial tendency, although Jellen *6 has reported 2 separate instances of affected sisters, and Crohn states he has seen the disease 3 times in siblings and believes this may indicate a common infective agent.

Careful search for the cause still meets with failure The most tenable theories indicate that a chronic low grade infection with lymph stasis is definitely concerned in the pathologic physiology of the snydrome as demonstrated experimentally by Reichert and Mathes.87 From this, Upham⁸⁸ concludes that regional enteritis is the result of a mesenteric lymphadenitis from some upper respiratory infection. The finding of bacteria in pure culture has been difficult Pemberton and Brown⁸⁹ found a pleomorphic streptococcus in only 1 of 4 cultures In the cases of Mixter.90 2 showed an anaerobic streptococcus Bacillary dysentery has been reported as a cause, but Bargen⁹¹ believes this only predisposes if it is present at all. The late William I Mayo was interested in the etiologic possibilities of bovine or avian tuberculosis. Frei tests were negative in 10 cases reported by Stafford,92 but the similarity of regional ileitis to lymphogranuloma inguinale makes this author believe a virus must be responsible

Symptomatology — To follow in sequence, it would probably be best to describe the clinical picture as seen in the 4 stages. Thus, in the acute stage, which according to Crohn⁵⁴ is rare, the symptoms are due to peritoneal irritation and mimic acute appendicitis. There is pain and tenderness in the right lower quadrant, accompanied by cramps, fever,

leukocytosis, and frequently a palpable mass. Usually it is safer to perform a laparotomy to be sure the condition is not one of acute appendicitis. If diseased ileum is discovered with a relatively normal appendix, most surgeons recommend closing the abdomen without any surgery.

In the later stages, the symptoms are suggestive of acute ulcerative colitis. There is diarrhea with cramplike abdominal pain and at times mucus but rarely blood in the stools. Severe anemia may develop with marked loss of weight, malaise, and a low grade fever These symptoms may have been present for a year or longer The disease gradually passes into the stenotic stage where the symptoms of partial small bowel obstruction with audible borborygmi are manifest. There are varying degrees of abdominal distention A mass in the lower right quadrant is invariably palpable. Violent cramps, occasional attacks of vomiting and constipation may occur.

One of the most marked features of the disease is the tendency to sinus and fistula formation as seen in the fourth stage. These are due to slow perforations of mucosal ulcers. Rarely is there an acute perforation Fistulous tracts may be many and diverse They are chemical or lytic in action due to seeping intestinal content and may travel wide distances. Internal and external types are recognized. In the former, the tract runs from the terminal ileum to other parts of the bowel, bladder or vagina. In the latter type, the sinus is from the ileum to the scar of a previous laparotomy run to the inguinal region, the lateral abdominal wall or to the right lumbar region Perianal, rectal and rectovaginal fistulas are the commonest Penner.93 writing with Crohn on perianal fistulae, are of local origin in the crypts of Morsays that most of them complicating ileitis gagni, but direct fistulization from ileum

to rectum or to perirectal spaces and then downward to the perineum may occur. Penner also states that all fistulae which occur in association with ileitis may precede the consciousness of an intestinal disturbance and therefore advises careful study of all cases of fistula-in-ano for ileitis. Prouty⁹⁴ and others, recognizing the slow progressive course of the disease toward bowel obstruction over many months and years through successive stages of infiltration, ulceration, stenosis, and fistulation, prefer to describe the symptoms from the acute and chronic angle only. All point out the inability to distinguish the first few attacks from acute appendicitis. Olson⁹⁵ finds that 50 per cent of the chronic cases have already had appendectomies.

Diagnosis—A diagnosis can only be inferred by a careful history of pain in the lower right abdomen when the ileum only is attacked, in both hypogastric and periumbilical regions if the jejunum is also involved, in the right hypogastrium and radiating upward if the colon is also diseased; distress for months or years made worse with food or relieved with defecation; low grade fever and a moderate leukocytosis; several bowel movements daily containing mucus and occasionally blood; distention and a fixed palpable mass; and above all the x-ray findings

X-rays are by far the most valuable and to a proper medical diagnosis of this condition. To Kantor⁹⁶ goes the credit for the most painstaking and exhaustive work. In addition to the technic of repeated exposures over a 9-hour period following ingestion of the opaque meal he has described 5 classical signs. First, a filling defect in the terminal ileum with a mild ileal stasis and distention proximal to the defect. Second, as the stenosis increases, a fine line of barium is seen in the ileocecal junction. This slightly irreg-

ular linear shadow, suggesting a cotton string extending more or less continuously from the region of the last visualized loop of the ileum through the entire extent of the filling defect and ending at the ileocecal valve, is the "string sign" of Kantor. Although considered pathognomonic by some of regional ileitis, Kantor denies this and points out that it must not be confused with a filled appendix dipping into the pelvis, a right sacroiliac synchondrosis or the streaklike filling of a spastic segment The third of Kantor's quintette is a filling defect just proximal to the cecum. His fourth observation is an abnormality in the contour of the last filled loops of the ileum and lastly the ileac loops just proximal to the lesion may show dilatation. Weber⁹⁷ relies more on the barium enema, believing the lowermost part of the ileum is best examined after it has been filled with contrast material in retrograde direction through the ileocecal orifice at the conclusion of the examination of the colon with the contrast enema He points out how the picture varies with the degree or stage of pathology In the early hyperplastic stage there is narrowing of the lumen due to encroachment on it by the more or less markedly thickened intestinal wall, shortening of the segment involved due to contraction of the hyperplastic tissue, loss of normal pliability and motility noted when the diseased intestine is manipulated. In the ulcerative stage narrowing, shortening, and rigidity of the affected segments are not so prevalent but there are revealing changes in the pattern of the mucosal relief as a flat moist stippled relief due to denudation of the internal surface Fistulae, when present, according to Weber, can be recognized without great difficulty.

Still another method of examining diseased bowel, especially when some degree

of obstruction is present, has become available since Miller and Abbott98 began their investigations of enteric functional activity, using 2 and 3 lumened tubes carried downward all the way to the ileum by peristalsis acting on an inflatable balloon. Abbott and Johnston⁹⁹ soon found by instilling a small quantity of thin barium suspension through the tube they were definitely able to locate and clearly visualize with x-rays the site of obstruction. It was then easy for Abbott¹⁰⁰ to adopt this method for the diagnosis of regional ileitis and thus remove any fears of causing a complete obstruction from the usual oral dose of barium. It is to be noted that this is a delicate technical procedure but the relative safety certainly warrants its careful consideration by all internists and roentgenologists.

In summation, to make a diagnosis, 3 cardinal features occur in 95 per cent of the cases as presented by Clark and Dixon. 101 (1) A mass in the lower right quadrant; (2) chronic intestinal obstruction; (3) positive roentgenographic findings

Differential Diagnosis — Recognizing by this time the protean nature of this disease, the difficulty in proper diagnosis becomes apparent Appendicitis, ulcerative colitis, and tuberculosis of the bowel are the most frequent diseases mistaken for ileitis. Recurrent attacks of appendicutes may never be completely separated from acute ileitis but certainly the surgeon should no longer make the mistake of removing a normal appendix through too small an incision to properly visualize the adjacent bowel and palpate its mesentery. Ulcerative colitis can be properly ruled out by its characteristic ulcers in the rectum and sigmoid as seen through the sigmoidoscope and by the definite x-ray findings of a pathologic Formerly the term tuberculosis of the bowel included most cases of ileitis but now primary intestinal tuberculosis is considered very rare. Thus in tuberculous enteritis careful search should elicit the primary focus. Chest x-rays, Mantoux skin test and examination of the feces for acid-fast organisms clinch the diagnosis of a Koch infection.

Weber states that, if in the x-rays an active chest focus coexists with a nonneoplastic lesion of the intestine below the duodenum, this is also tuberculous. The reverse of this, in general, is also true. The difficulty in separating the diseases of the ileocecal region as seen by the radiologist can be appreciated when one realizes that, according to Jellen¹⁰² in his treatise of this subject, there are some 44 types of lesions to be considered.

Crohn believes it is rare to fail in the diagnosis by x-rays and believes if the findings are negative then other causes of the diarrhea must be sought. An elevated basal metabolic reading may reveal a thyrogenic cause. Similarly, achylia may reveal a gastrogenic cause. Likewise diarrhea due to food allergy, nervous or emotional states requires due consideration in evaluating intestinal hypermotility. Nontropical sprue is hard to differentiate from high ileitis as the x-ray picture is not constant and consists only of delays and puddling in the higher loops of the ileum and jejunum. The stools in sprue are frothy and do not contain blood, whereas in ileitis they are more purulent and do contain blood.

Carcinoma anywhere in the gastrointestinal tract must be considered but usually it will involve the cecum in older individuals without intermittent attacks and by x-rays gives a shorter more abrupt demarcation with a deleted mucosal pattern. Other conditions, as lymphogranuloma inguinale, Meckel's diverticulum, diverticulitis, actinomycosis,

foreign bodies, Hodgkin's disease, and amebic granulomas, must be mentioned.

Clark discusses the laboratory examinations used at the Mayo Clinic for making a differential diagnosis Stools are examined for Bargen's diplostreptococcus, dysentery bacillus, myobacterium tuberculosis, ova, parasites (ameba), blood and pus. The blood is tested for lues, dyscrasias, undulent fever, and tularemia. Mantoux and Frei tests are performed In addition to a small bowel progress study, the chest is x-rayed for tuberculosis. If fistulas are present, the pus and scrapings are examined for actinomycosis, blastomycosis, and tuberculosis.

Treatment—In the acute stage, since most diagnoses are made at operation for suspected appendicitis, there is no medical therapy indicated, but if the appendix is found normal, Crohn, Mixter, Jones, 10.3 and others agree to close the abdomen without removing the appendix and emphatically without drainage because of the risk of fistula formation Then conservative medical treatment should be carried out for 3 to 6 months In the chronic stage, a bland, high caloric, high protein, high vitamin, low residue diet is indicated. Added vitamins, liver and iron, small blood transfusions, vaccines, and bacterins are used. Symptomatically, bismuth, antispasmodics, and sedatives will have to be given. Bassler¹⁰⁴ reports recovery of 21 patients with repeated x-ray exposures but there is no confirmation of this rather startling work

All authorities recommend surgery as the most promising curative measure but by no means are they in accord on just what to do. Obviously, this decision cannot always be made until the extent of the lesion is ascertained. According to Crohn, Berg, Brown, Bargen, Weber, Mixter, and others, a *1-stage resection*

is the operation of choice, with complete removal of all the diseased area and a liberal portion of the mesentery. An end-to-side ileocolostomy is done and the abdomen in most instances is closed without drainage. If the patient is a poor risk or the disease unusually fulminating, a short-circuiting or sidetracking anastomosis is performed with the idea of doing a second stage resection at a later date when the patient's condition has improved. Dixon¹⁰⁵ is very much in favor of this 2-stage procedure

On the conservative side, Kross¹⁰⁶ believes that in early cases radical resection is unnecessary and conservative procedures indicated. He reports 3 cases, in 1, only an appendectomy was done with no recurrence after 5 years; the second had an enterostomy with no recurrence 4¾ years later, a sidetracking was done in the third with no recurrence after 1¼ years. Pemberton and Brown find no progress of the disease before 6 months if a short-circuiting operation is done. Meyer and Rosi observe symptoms relieved in 50 per cent by a sidetracking operation alone.

Colp¹⁰⁷ admits surgical treatment is far from standardized and that the efficacy of the various procedures employed will be determined and correctly evaluated only after careful follow-up examinations have been made over long periods of time. He with Abbott admits there may be recurrence even after rather extensive resection. For the complications most agree to do 1- or 2-stage radical resections and find even perianal fistulae will usually close without direct attention.

Mention should be made of the medical management of the surgical cases. Two important features have been frequently overlooked (1) The correction of nutritional deficiency; and (2) keeping the intestine decompressed. According to Casten, ¹⁰⁸ nutritional disturbances

so extensive as to be a direct factor in the ultimate outcome have not been reported and even lesser degrees of deficiency in nutritive elements are only occasionally mentioned in passing. 101 He states that the severe diarrhea, extensive involvement of absorptive areas, dietary restrictions and natural food aversions all cause extensive changes in body nutrition. To overcome this hypoproteinemia (with actual lowering of plasma protein level) and avitaminosis he recommends the forcing of protein by mouth, transfusions of whole blood or plasma and an adequate schedule of vitamin administration. The problem of distention has recently been very successfully handled, according to Clark, 101 by the inhalation of high concentrations of oxygen (95 per cent).

Course and Progress—Typically, the disease is chronic, running a course of several years but it may run the entire range of inflammation to stenosis and fistulae in a few weeks. Obviously, the prognosis varies with the stage in which the disease is first encountered. Undoubtedly, properly diagnosed cases have resolved spontaneously, especially when

seen in the acute phase. Crohn¹⁰⁹ reports 17 nonoperated cases with a mortality of 17.6 per cent, whereas in a series of 51 operative cases, the mortality was only 9.8 per cent and concludes the risk to be twice as great when surgical aid is refused. In the acute cases where the indications for surgery are by no means clear, Crohn⁸⁴ has reported 11 cases. Three have apparently done well without treatment, 8 poorly, and 6 were eventually operated on.

Surgery is mandatory in the chronic cases but the prognosis of the 2 main types of technical intervention must be considered. In the radical resection group, Crohn reports only 1 mortality out of 32 cases. With the palliative or short-circuiting procedure, the immediate risk is less but cure of the disease not likely (although Lewisohn and Colp report favorable results) and the risk at a later resection greater. Mixter,90 through a questionnaire, gathered 363 cases of which 278 had major operations with a mortality of 14 per cent and a recurrence in 20 per cent Twenty-five of the 27 surgeons responding approved of radical resection.

SMALL INTESTINAL INTUBATION

By W OSLER ABBOTT, M D.

This article deals with intubation of the small bowel distal to the duodenum. The problems involved in the procedure are in the main sufficiently different from those of duodenal drainage to make it a separate subject.

The first passage of a tube from mouth to rectum was accomplished in 1908 by Sheltema, 110 a pediatrician of Gronigen, who used a thin rubber tube of 3.8 mm. diameter weighted with a ballbearing. After several days, the tip appeared by

rectum He spoke of treating intestinal parasites by such a tube but he did not consider the withdrawal of contents to be practical. In 1919, Einhorn¹¹¹ repeated this procedure, using a still smaller tube (26 mm diameter) and was likewise unable to aspirate gut contents. Buckstein, ¹¹² in 1920, used such a tube for the injection of barium in the course of roentgenographic studies of the duodenum and upper jejunum. In 1920, McClendon¹¹³ made the first satisfactory

collections of gut contents, using 2 normal subjects over a period of days. In 1921, Einhorn¹¹⁴ reported treating 1 case of ulcerative colitis by injections into the cecum. Later he treated 2 more cases, requiring 7 days and 6 days, respectively, to reach the colon.

Jones and Pierce¹¹⁵ in 1931 attached a balloon to a tube and studied the sensa-

on the contents of the normal gut have been amplified by Karr and Abbott,¹¹⁷ by Miller and Karr,¹¹⁸ by Owles,¹¹⁹ and by Groen.¹²⁰ The absorption of glucose was studied by Groen,¹²⁰ by Abbott, Karr and Miller,¹²¹ and by Shay, Gershon-Cohen and Fels.¹²² Drug effects on the intestine have been reported by Miller and Abbott,¹²³ Abbott and Pen-

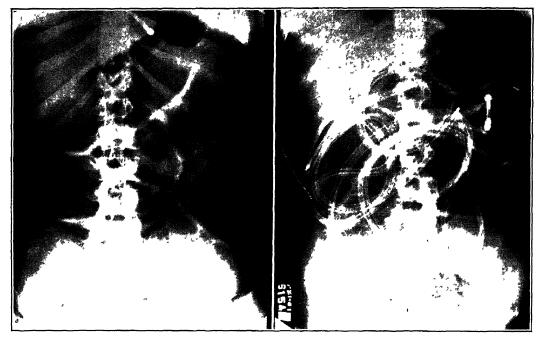


Fig 1—Mechanical intestinal obstruction Case V B Left, marked small intestinal distention was present before intubation Right, decompression of the abdomen following the passage of a No 14 F and a No 3 F tube (Abbott and Johnston: Surg, Gynec, and Obst)

tion produced at different levels throughout the gut by producing local distention. Miller and Abbott¹¹⁶ in 1934, by using a terminal balloon on a double lumened tube, or on 1 of 2 tubes, were able not only to intubate the entire small bowel, but to sample the contents at will from the stomach to the cecum. The most important single feature of this technic was the use of the balloon for, by keeping it constantly inflated, the time required to reach the colon was reduced from several days to a few hours. This immediately made possible many studies of small intestinal function. McClendon's observations

dergrass,¹²⁴ Abbott and Henry,¹²⁵ and by Elsom and Drossner ¹²⁶

The first important clinical use of the technic, however, was reported by Abbott and Johnston¹²⁷ after a 3-year experience with the method in the treatment of acute intestinal obstruction. The way for this development had been laid by Wangensteen and Paine¹²⁸ in their epoch-making paper of 1933, in which they pointed out the great therapeutic value of gastroduodenal drainage in tiding some patients over an episode of acute obstruction and as a preoperative procedure for others. An appreciable

lowering of the mortality rate in this condition resulted. It is to Wangensteen and his associates that we owe the demonstration of a diminishing death rate in acute bowel obstruction even if the stomach alone is kept continuously aspirated for some hours before operation, and certainly while the patient's disturbed fluid. electrolyte, and protein balances are

i. e., a balloon for peristalsis to propel along the gut, a passage for inflating the balloon, and a passage for aspirating the intestinal contents, or for the injection of solutions.

Many variations of this basic equipment have proved satisfactory. Abbott and Johnston¹²⁷ used (1) a double lumened tube with a terminal balloon and

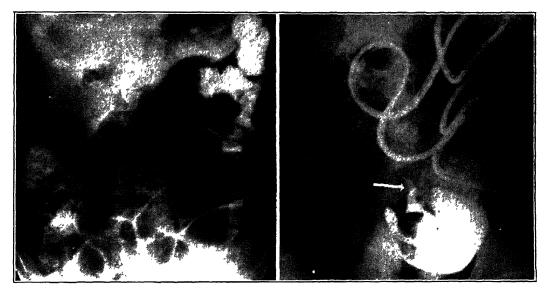


Fig 2—The localization of a mechanical obstruction. Case W. S. Left, small intestinal distention was marked prior to intubation. The colon is outlined by the unexpelled residue of a barium enema. Right, the small intestine has been decompressed by the passage of a No. 14 F and a No. 3 F tube. Barium has been injected down the tube and has regurgitated up a dilated loop of ileum. Its advance is blocked by a point of narrowing (arrow) just distal to the air-filled balloon and the tip of the tube. (Abbott and Johnston. Surg., Gynec. and Obst.)

being readjusted. He points out, however, that the defects in gastroduodenal drainage alone are twofold, (1) the faulty mechanical principle involved in aspirating from the upper rather than the lower end of the obstructed portion of the gut, and (2) the impossibility of feeding the patient while the gastric tube is in place. It is because these 2 faults are remedied by the use of the 12-foot small intestinal tube that a still further reduction in the death rate from acute intestinal obstruction has been brought about

Method—(1) **Apparatus** — The essentials of the method as described by Willer and Abbott¹¹⁶ remain unchanged,

suction proximal to it, (2) a double lumened tube with suction applied ahead and behind the balloon, and a tip 1 cm long and the same caliber as the tube, (3) 2 tubes together with a Twiss tip extending several centimeters ahead of the balloon and suction applied immediately ahead and behind, (4) 2 tubes with an Einhorn "bucket" ahead of the balloon and aspiration holes in the tube behind, also

In subsequent papers, Johnston, Penberthy, Noer and Kenning¹²⁹ have almost uniformly used this last¹¹³ arrangement, while the second¹¹¹ has been used more frequently by Abbott¹³⁰ and almost

exclusively by Wise,¹³¹ Fisher,¹³² and Leigh, Nelson and Swensen.¹³³ Abbott¹³⁴ subsequently found it useful at times to have the balloon 2 or 3 centimeters ahead of the aspirating tube. Wilson¹³⁵ prefers the catheter tipped tube with suction applied ahead of the balloon only. Many other variations are constantly being suggested.

My own experience would indicate that a stiff tube with the balloon, 3 to 5 cm. back from the tip and with the tip itself tapering or at least not enlarged can be more rapidly manipulated into the duodenum than can a limber tube with only a small tip ahead of the balloon, but once in the jejunum it will advance more slowly and intermittently. When multiple partial obstructions are present, a tube with the balloon 3 cm. ahead of the aspirating tube, while hard to place in the duodenum will be less easily arrested in its progress. For extremely ill patients or those who because of injury or operation cannot be moved, a limber tube with a large duodenal bucket will most readily gravitate into the duodenum.

Any suction apparatus that can maintain a 5-foot negative hydrostatic pressure evenly over a period of time is satisfactory. Wangensteen's bottles are generally the most useful

(2) Procedure—The technic of passing a long tube in the presence of an obstruction to the small intestine has been described by the same authors who have described the equipment. All are agreed on the basic principle of inserting the tube with the balloon empty to the midpoint of the duodenum and there distending the balloon to a degree that will allow peristalsis to propel it forward. The steps by which this is accomplished have varied in different hands. It is generally agreed that the tubes should be passed through the nose if possible so that the patient may eat more easily.

The tube readily enters the stomach but because of the tight constriction of the antrum generally present in this condition it coils to the left. Abbott and Johnston¹²⁷ have advised distending the stomach to smooth out the rugae and open the antrum.

The injection of 200 to 300 cc. of air with the patient on the right side of his abdomen allows the tip to drop to the pylorus at once. If his illness, injuries or recent operation preclude this, the stomach may be filled with water and the tube floated to the pylorus by the injection of a little air into the balloon The stomach should be emptied as soon as the tip has traversed the antrum. This can be done in bed with reasonable assurance that the tip will reach the pylorus. For greater certainty, it may be carried out under a fluoroscope, though if this is done the patient should be brought on a litter and the mattress, patient and bedding lifted together to the fluoroscopic table The tube may be seen quite adequately and the patient is saved exhausting discomfort Under fluoroscopic guidance it is often possible to pass the tube immediately into the duodenum, though, in the majority of cases, the tube is advanced to the pylorus only and the patient left upon his right side in bed

Wilson¹³⁵ stresses the value of gastric lavage in helping to enter the duodenum but does not use manipulations under the fluoroscope. In our own hands, lavage with 0.9 per cent *NaCl* and with hot 1.5 per cent *NaHCO*₃ solutions has occasionally helped, as has the use of nitroglycerine, atropine, trasentin, and benzedrine on different occasions when injected down the tube in 10 cc of water, but none of these drugs has consistently facilitated the process.

The time required to place the tube in such a position that the balloon can be blown up varies from the immediate results often obtained by manipulation under the fluoroscope (Abbott and Johnston) to 2 to 6 hours for Wise and about 12 hours for Wilson. In this connection, however, it is worth considering the notable success achieved by Wangensteen¹³⁶ with gastroduodenal drainage only and the finding of Penberthy, Johnston and Noer¹³⁷ that 46 per cent of their advnamic ileus cases were relieved before the tube traversed the duodenum My own practice at the present time is to leave the tube with the tip in the pylorus as long as the patient is improving. This has been for 24 or even 48 hours in rare cases, but has eventually led to satisfactory intubation and decompression of cases that would have been very bad surgical risks otherwise.

Having left the tip in the pylorus with adequate slack in the stomach, the next point is to determine when it has entered the duodenum Fluoroscopy or a roentgenogram gives the surest answer. When this is not immediately available, much can be told by the feel of the balloon as one injects air into it, if the air passage is not too small and if the syringe is large (50 cc), dry and smoothly ground. The stomach offers little resistance to the inflation of a balloon save in a patient with great distention and then the plunger, when released after the injection of 20 cc of air is driven back rhythmically with every inspiration. The pylorus offers a strong rubbery resistance. The duodenum, however, offers less resistance but expels the syringe plunger irregularly and without relation to respiration. While severe illness confuses the sharp difference between these responses the point is often of great value

Having reached the distal portion of the descending duodenum, air may now be injected with confidence that the balloon will advance. The volume recommended varies from 25 cc to 30 cc ¹³⁴

to 40 to 60 cc.¹²⁹ An 8 per cent sodium iodide solution in the balloon was used but early abandoned by Miller and Abbott,123 but has subsequently been recommended again by Wilson. 135 The advance of the tube now continues until an obstruction is reached, the air withdrawn from the balloon or the balloon expelled by rectum. The speed at which the tube should be swallowed has been given as 6 inches per hour 130, 131 and 1 cm. every 5 minutes.¹³⁵ The point of real importance, however, is that the tube be not passed into the fundus more rapidly than the small gut is pulling it out through the pylorus or the slack will coil in the stomach. By avoiding pressure on the tube sufficient to gag the patient as it is being inserted through the nose, one avoids this difficulty

Irrigation of the tube to avoid clogging of the lumen should be done with saline at intervals of 1 to 3 hours, depending on the thickness of the material aspirated.

To withdraw the tube even from the cecum, it is necessary only to empty the balloon and make gentle traction A foot of tube every 5 minutes may be recovered.

Uses of Intubation—(1) Control of Food, Fluid and Electrolyte Balance —An intubated patient may be brought more quickly into a good fluid and electrolyte balance because one can more accurately determine the amounts lost and replace them by intravenous infusions. Very soon after the obstructed gut has been emptied, however, the patient may be fed by mouth, and if the major portion of the small gut is above the lesions, a completely obstructed patient may be kept for weeks in a good state of nutrition. This is of inestimable value in handling inflammatory obstructions. Abbott134 has shown that the salt content of the drainage averages about 0.5 per cent and salt replacement by vein should

exceed this figure somewhat. The need for fluid and protein replacement is too well appreciated to call for comment here. Note has been made by Noer and Johnston, ¹³⁸ and by Abbott, ^{130, 139} of the foods which may be eaten with least danger of the tube becoming clogged. These may be roughly described as composing a high protein, low cellulose diet. Johnston, *et al*, ¹²⁹ and Fisher ¹³² have each maintained patients as long as 22 days in this fashion.

- (2) Relief of the Obstruction—The experiences of Wangensteen¹³⁶ with the shorter tube in seeing clinically complete obstructions spontaneously reduce themselves following decompression have been frequently duplicated by those using the long tube ¹²⁷, ¹²⁹, ¹³⁰, ¹³⁴, ¹³⁷
- (3) Identification of the Lesion-A most important use of the procedure is in making possible roentgenological diagnosis with the aid of injected barium sulfate which, if the obstruction is complete, may be withdrawn again. This has not only been stressed by Abbott and Johnston, 127 Chamberlain, 140 Lofstrom and Noer, 141 and others in the severe cases, but as stated by Abbott and Johnston127 and by Abbott130, 139 minimal lesions of the gut, even when so slight as to be difficult of detection by an opaque mouth meal, may also be detected by intubation. This has been further confirmed by Boon 142
- (4) The Surgical Technic Is Simplified—The point has frequently been stressed that preoperative decompression of the gut has simplified the surgery of intestinal obstruction tremendously. The eradication of gas and fluid filled loops from the operative field has been important and the relief of intraintestinal pressure upon a suture line following a resection has been stressed as having reduced the danger of leakage.

Contraindications—(1) All authors have agreed that the successful use of intubation must depend upon the accuracy of the initial diagnosis of the presence or absence of strangulation as no measure delaying surgery in the presence of this complication is ordinarily justifiable. It is noteworthy, however, that Johnston¹⁴³ has suggested intubation as preferable to surgery when the diagnosis of mesenteric artery thrombosis can be made with some assurance and Leigh¹³³ has used it in 5 cases with gangrene of the gut in conjunction with surgery.

- (2) Obstructions of the colon have been found difficult to cope with by intubation, though it occasionally proves of great help here also.
- (3) The danger of intubation in the presence of a cough productive of sticky sputum has been stressed.
- (4) Erosions of the throat have been reported in a few instances, but in some at least they were probably the result of the use of too much tension in withdrawing the tube.

Results of Intubation—Activity is restored by decompression even when paralysis has already resulted. This occurs without regard to whether the paralysis results from peritonitis, spinal injury, trauma to the intestine or a mechanical obstruction (Abbott and Johnston, 127 Johnston, 143 Wise, 131 Johnston, et al, 129 Noer and Johnston, 138 Abbott, 130, 134, 139 Fisher, 132 Penberthy, Johnston and Noer, ¹³⁷ Leigh, Nelson and Swenson ¹³³). Penberthy, Johnston and Noer¹³⁷ report 19 postoperative adynamic ileus cases without gross infection All were decompressed (8 by gastroduodenal suction alone) and all lived. Eleven patients showed extraperitoneal inflammation, toxemia and trauma Six died, 4 in spite of decompression. Twenty-four patients had peritonitis with or without operation Six died, 4 of them in spite of decom-

pression. The mortality for the entire group of 54 cases was 22.5 per cent with 93 per cent of them successfully decompressed. Leigh, Nelson and Swenson¹³³ report 12 cases of paralytic ileus, all decompressed with the long tube and all recovering. They have treated 38 patients having mechanical obstructions without gangrene with 1 death (mortality 2.7 per cent). Johnston, et al., 129 in a group of 54 patients having either mechanical or paralytic obstruction, or both, had a mortality of 9.3 per cent. In this group 9 other patients died from causes unrelated to their obstruction. Abbott and his co-workers have treated 75 cases of

frank obstruction, 48 in the small bowel, with an equal division between the inflammatory and noninflammatory lesions and a gross mortality of 19 per cent. In 23 the obstruction was of the large bowel, all but 3 of them being noninflammatory, and the gross mortality was 22 per cent. These figures include many patients referred to us when already in extremis from peritoneal carcinomatosis, tuberculosis, general peritonitis and postoperative pneumonia with ileus. A close analysis of the 16 deaths in the light of our present experience suggests that 3 might be said to have died primarily of intestinal obstruction.

VITAMINS

By John H. Willard, M.D.

Youmans¹⁸² has emphasized the lack of accurate knowledge regarding the effects of deficiencies on diseased states other than primary avitaminoses. Most of the accepted work has dealt with the effects of vitamins in definite deficiency diseases, such as scurvy, pellagra, and beriber: While "there is good reason to believe that vitamin deficiencies occur as complications of many diseases and modify unfavorably their course and outcome," the proof of such relationships is not at hand Until such proof is obtained, the promiscuous use of vitamin concentrates is unscientific Fortunately, however, harmful effects are very seldoni noted McLester, 183 in discussing borderline nutritional states, concludes that dependence should be placed on an adequate diet rather than on vitamin concentrates. However, with definite indications, concentrates may be necessary and then should be used in sufficient quantity.

Vitamin A

Sources:

- 1 Eggs, milk, butter, green and yellow vegetables.
- 2 Fish liver oils, carotene

DAILY REQUIREMENTS

3000 to 8000 international units

SYMPTOMS AND SIGNS OF DEFICIENCY

Night blindness, keratinizing metaplasia of epithelial cells (cornea, bronchi, skin, renal pelvis, etc.).

Diagnosis

History, biophotometric readings, epithelial scrapings, blood determinations

CAUSATIVE FACTORS

- 1 Insufficient intake.
- 2 Faulty absorption (jaundice, small bowel disease, celiac disease)
- 3 Faulty storage (liver disease)

TREATMENT

Oral—Cod liver oil, halibut liver oil, carotene
Inunction—Cod liver oil

Intravenous—Carotene

It has been well established that vitamin A is essential for the health of epithelial tissues. Deficiency of this factor

results in replacement of normal cells by keratinized cells with resultant loss of normal functions. Decreased resistance to infection may follow. One of the outstanding functions of vitamin A is concerned with retinal activity. Deficiency results in decreased function of both rods and cones causing some degree of night blindness.

Requirements — Booher^{144, 156} has shown that the average requirement of this vitamin to prevent night blindness is between 25 and 55 units per kilogram of body weight per day. The carotene requirement is about twice this amount. An adequate safe intake of vitamin A would be about 3000 units. For growing children and pregnant women, the intake should be increased to 5000 to 8000 units.

Diagnosis of Deficiency—Since the clinical use of the biophotometer as a measure of vitamin A deficiency was introduced by Jeans and Zentmire in 1934, there has been considerable discussion of the reliability of this test Isaacs, Jung and Ivy145 found no definite correlation between biophotometric determinations and vitamin A intake Hecht and Mandelbaum, 146 using a special adaptometer, measured rod and cone light thresholds and found that wide variations are present in normal individuals. Their experiments do not bear out the hypothesis that these differences are always dependent upon the vitamin A content of the body or the diet. Five of 6 patients showing abnormal dark adaptation were not affected by large doses of vitamin A. The authors suggest that the difference between their results and others may be in the apparatus and the technic used.

Four normal individuals were placed on low vitamin A intake and showed a steady rise in both rod and cone thresholds. Rapid decrease in these levels occurred when normal diets were resumed or when vitamin A was added. They conclude that, under strictly standardized conditions, measurement of dark adaptation can be used as an aid in the diagnosis of avitaminosis A, but they question the reliability of the simple biophotometric determinations previously advocated.

In contrast to the relationship between vitamin A intake and dark adaptation shown by these writers and by Wald, Jeghers and Arminio, 147 Steffens, et al. 148 have reported failure to demonstrate a change in adaptation after deficient intake of vitamin A for several months. In 1 case, skin changes (hyperkeratosis) appeared before notable changes in dark adaptation. These writers suggest that in some individuals sufficient storage of vitamin A may occur to maintain normal visual function for long periods.

Tissue sections and scrapings from epithelial surfaces have been shown to be a fairly reliable test of vitamin A deficiency

To date no simple reliable laboratory test for blood content of vitamin A has been introduced. Kimble¹⁴⁹ using the rather complicated photocolorimetric method of Dann and Evelyn, found that this procedure gave consistent results and that vitamin A in plasma was quite stable but did not report clinical studies. A relationship between blood fats, carotene, and vitamin A has been shown by Josephs ¹⁵⁰

Causes of Deficiency — Vitamin A deficiency may result from insufficient intake, faulty absorption, as in jaundice and small bowel disease, or from faulty storage resulting from hepatic disease

This latter subject recently has been studied by Patek and Haig ¹⁵¹ Previous reports dealt largely with jaundiced patients where the factors of faulty absorption and insufficient intake probably played an important part. These authors

studied 24 patients with cirrhosis of the liver but without jaundice. Abnormal dark adaptation readings were found in 19. Administration of vitamin A resulted in some improvement but evidence of deficiency persisted. They conclude that "abnormal dark adaptation in patients with cirrhosis of the liver is due chiefly to altered intermediary metabolism of vitamin A."

The possibility that administration of mineral oil may interfere with absorption of vitamin A has received considerable attention Curtis and his associates^{152, 153} demonstrated that mineral oil by mouth, if taken during the day, decreased absorption of carotene Emulsions of mineral oil had the same effect. Nightly doses had little if any effect Since the average person obtains most of his vitamin A by conversion of carotene absorbed from the diet, the authors believe this observation to be of importance. Saturation at body temperature of the mineral oil product with carotene prevented the loss of this material from carotene containing foods

Relation to Urinary Lithiasis — Since epithelial changes may be of etiologic importance in urmary calculi and since renal calculi occur in vitamin A deficient rats and guinea pigs, several writers have studied the possible relationship between vitamin A deficiency and this condition. Long and Pyrah¹⁵⁴ quote Ezickson and Feldman as finding photometric evidence of A deficiency in 24 of 25 patients. The former authors studied 25 patients with calculi and 65 controls. In the stone group, 40 per cent had disturbed dark adaptation, while none appeared in the controls However, 42 per cent of the calculous cases showed normal readings. Administration of large doses of vitamin A did not result in The possibility of inimproved tests creased excretion of vitaniin A was ruled out by careful urinary studies. It was concluded that in many cases of urinary calculi there was a disturbance in absorption or in conversion of the precursors of vitamin A.

Ezickson¹⁵⁵ studied liver function by means of the bromsulfalein test in 39 patients with urinary lithiasis Using a dosage of 5 mg. per kg. of body weight, it was found that most of the patients had retention of dve after one-half hour varying from 14 to 60 per cent. Tests done in 1 group on a nonfasting basis showed 50 per cent to have retention, while in a fasting group 90 per cent showed retention. Biophotometric readings indicated that 94 per cent of these patients were deficient in vitamin A. The author suggests liver dysfunction as a possible cause of faulty absorption and storage of this vitamin or its precursor carotene.

Vitamin B Complex

Sources

- Whole grams, egg yolk, liver, leafy vegetables, yeast.
- 2 Yeast extract, liver extract
- 3 Synthetic
 - (a) Thiamin
 - (b) Nicotinic acid
 - (1) Riboflavin
 - (d) B₆

REQUIREMENTS

- 1 B₁—200 to 300 International Units (1 mg Thiamin)
- 2 Nicotinic Acid—?
- 3 Riboflavin—3

SYMPTOMS AND SIGNS OF DEFICIENCY

- B₁—Beriberi Anorexia, glossitis, achlorhydria, anemia, diairhea, peripheral neuritis, cardiac decompensation, edema
- 2 Nicotinic Acid—Pellagra Loss of weight, strength and appetite, mucous membrane lesions; glossitis, vaginitis, colitis, characteristic skin lesions, mental symptoms, diarrhea
- 3 Riboflavin—Cheilosis.

CAUSACINE FACIORS

- 1 Insufficient intake.
- 2 Alcoholism

- 3. High carbohydrate intake.
- 4 Increased metabolism (hyperthyroidism, pregnancy, fever).
- 5 Increased excretion (diuresis, diarrhea). Diagnosis:
 - 1. History and physical examination.
 - 2 Urinary excretion of B₁.

TREATMENT

- B₁—1. Twenty to 100 mg. thiamin per day.
 - 2. Thirty Gm. potent yeast T.I D.

Nicotinic Acid:

- 1. Oral 50 to 100 mg. 5 or 6 times daily (Spies).
- 2. Intravenous 10 to 20 mg.

Riboflavin—Three to 60 mg per day orally B₆—Fifty mg subcutaneously in N. S S

Attention has been called repeatedly to the frequent association of deficiencies of several vitamins Such multiple deficiencies are the rule rather than the exception. This is particularly true of the various factors included in the term B complex It has been shown, for instance, that pellagrins with psychoses and digestive symptoms may respond promptly to nicotinic acid but continue to show evidence of beriberi, riboflavin deficiency, scurvy, or vitamin A deficiency 157 These syndromes respond to specific medication. In dealing with any recognized symptom complex, such as beriberi or pellagra, one must not expect a clear cut picture of a single deficiency

Daily Requirements—Cowgill¹⁷⁶ estimated normal requirements as being about 10 units per 100 Calories of food intake. In case of excessive demand as in increased metabolism from thyroid disease or fever or in excessive loss from diarrhea or diuresis, the dosage may have to be increased to 15 to 20 units per 100 Calories of intake. The average requirement would be adequately met by 1 mg. of thiamin (300 units).

Determination of Deficiency — As yet no satisfactory clinical method of measurement of B_1 deficiency has appeared in the literature. The rat brady-

cardia test is complicated and of doubtful accuracy. Because of the reported increased blood content of pyruvic acid in beriberi, Wilkins, et al, 158 developed a type of pyruvic acid tolerance test. Measurements of the bisulfite binding substance (B. B. S.) of the blood were made before and after oral or intravenous administration of sodium pyruvate. While there seemed to be a tendency toward delayed removal of this substance from the blood in vitamin B deficient subjects, the differences were too small to be clear cut.

Joliffe and his collaborators¹⁶¹ measured urinary output by the method of Westenbruck and Grudsmit. This entails the use of a fluorimeter and comparison with a series of thiochrome standards.

Effects of Deficiency—Shattuck, 159 Vedder¹⁶⁰ and others have shown that the nervous system changes in beriberi are not primarily peripheral nor do they represent a true neuritis. They are in the nature of a toxic neuropathy and are most marked in the cord and the sympathetic ganglia The so-called polyneuritis of beriberi and that seen in alcoholism, pregnancy, chronic wasting diseases, and in prolonged febrile states are probably all of this type. In the circulatory system, deficiency of vitamin B₁ produces cardiac dysfunction secondary to hydropic degeneration of the muscle and to effects on the vagus nerves Other vascular changes may be present as a result of sympathetic ganglia changes The symptoms include tachycardia, palpitation, and fatigue Edema is a common finding in B₁ deficiency and has not been explained. An associated hypoproteinuria, with decrease particularly of the albumin fraction, may be the explanation. It has been found that sodium is particularly poorly borne in these patients The gastrointestinal symptoms in this type of deficiency consist primarily of anorexia, although nausea and vomiting and diarrhea may occur. This effect may be dependent largely on changes in the sympathetic nervous system. The exact mechanism of B_1 activity is not known but evidence at hand links this material with complete carbohydrate metabolism and with the activity of acetylcholine on the parasympathetic nerves.

Further information regarding vitamin B₁ deficiency was obtained by Jolliffe, et al.161 Urinary excretion of thiamin was measured by a fluorimeter in patients on carefully controlled intake of vitamin B₁. Records were kept of subjective symptoms, electrocardiograms, basal metabolic rates, blood chemistry, blood counts, and teleoroentgenograms On diets furnishing 43 to 63 per cent of adequate amounts of B₁, according to the Cowgill formula, subjective changes were noted in from 4 to 13 days These consisted of fatigue in 5, anorexia in 4, dyspnea on exertion in 3, precardial pain in 3, burning of the feet in 3, and leg cramps in 2 patients All of these symptoms disappeared after 3 days of adequate B₁ intake, administered without knowledge of the test subjects. Objective signs were hyperesthesia of feet and calves in 4, and electrocardiographic changes in 2 patients These also disappeared after 3 to 6 days of adequate vitamin intake. The urinary excretion was found to be proportional to intake Symptoms of deficiency did not occur until output reached about 30 per cent of the control excretion. From the figures obtained, these writers estimate that symptoms of deficiency would appear in from 4 to 11 days on a completely deficient diet

The value of *thiamin* in the *treatment* of polyneuritis has been studied by Vorhous ¹⁶² The diagnosis of polyneuritis depended on: (1) Recurrent attacks of pain in peripheral nerve areas in more

than 1 part of the body; (2) pain of more than 1 month's duration and in several attacks; (3) presence of paresthesia and muscle weakness; (4) neuromuscular tenderness (Valleix's points), and (5) changes in reflexes and reduced vibratory sense. The patients were given a daily dose of from 3 to 10 mg. of thiamin. Seventy-five per cent were treated orally, the remainder intravenously. In all, 520 patients were observed over a period of 5 years with the following results: 3 per cent unimproved; 36 per cent partially improved; 61 per cent symptom free while under treatment Recurrences were frequent as may be seen in the following table:

TABLE I Per Cent Recurrences

170 cases followed to 1 year . . . 21 111 cases followed for 1 to 2 years. 71 95 cases followed for 2 to 3 years. 85 123 cases followed for 3 plus years 96

This author believes that certain individuals require more vitamin B₁ than others and that this need is not met by what appears to be an adequate normal diet. He suggests the term "Primary Hypothiaminosis" for this group of individuals.

Aring, et al, 184 state that in severe deficiency disease with neuritic symptoms, biopsies have shown marked loss and degeneration of myelin sheaths. Under treatment with large doses of thiamin, regeneration occurs much more slowly than clinical improvement indicates. Experimental work is cited which suggests that thiamin enhances the transmission of nervous impulses by inhibiting the action of cholinesterase, a humoral effect which precedes anatomic change. These authors believe that thiamin is of value only in those cases in which deficiency is present and offer a table classi-

TABLE II
PRINCIPAL CAUSES OF NEURITIS

NEURITIS LOCALIZED NEURITIS GENERALIZED POLYNEURITIS Mechanical Infectious Deficiency or Chemical Virus Bacteriotoxic Pressure Diphtheria Mercury Measles Focal infections Metabolism "Rheumatism" Lead Tumor Tetanus Pellagra Smallpox Edema Streptococci Chickenpox Erysipelas Pernicious Silver Arsenic Arthritis Leprosy Scarlet fever anemia Parotitis Fibrosis Rheumatic fever Sprue Phosphorus Herpes Methyl alcohol Trauma "Acute febrile" Beriberi Chorea "Alcoholic Ethyl alcohol Saturday night "Acute Septicemia neuritis" Ethyl 10dide paralysis Infective" Puerperal fever "Korsakoff's "Laundry's" Trichloroethy- $\mathbf{Volkmann}$ Gonorrhea psychosis" contracture Poliomyelitis Meningitis lene Pernicious Carbon Meralgia Encephalo-Diphtheria myelitis vomiting tetrachloride paresthetica Typhoid **Epidemic** Hunger edema Trinitrotoluene Paratyphoid Dinitrobenzene Pregnancy (lethargic) fever encephalitis Chronic colitis Triorthocresyl Typhus fever Cancer with phosphate Erythredema Influenza Acute rabic Pneumonia cachexia Anılıne Tuberculosis Sulfonethylmemyelitis Malaria with cachexia than, barbital Relapsing fever Chloral hydrate, Serum sickness Senility with chlorobutanol cachexia Acute enteric Diabetes Carbon monoxide fever Carbon disulfide Syphilis Myxedema Hematoporphy-Thallium rınuria Sulfur Recurrent Emetine polyneuritis" Gold Bismuth Chronic progressive poly-Sulfanılamıde neuritis' Chronic bacil-

lary dysentery

fying the types of neuritis. While some improvement has been noted by others in various types of neuritis, the authors feel that the primary usefulness of thiamin is in the deficiency or metabolic group. They recommend 50 to 100 mg per day given parenterally in doses of 10 to 20 mg. If no response is obtained in 1 week, further thiamin therapy will be useless.

Gout has been treated by thiamin injections by Callahan and Ingham¹⁶³ with favorable results. They used 4500 to 9000 international units daily

Vitamin B₂ or G—Many factors have been described under this heading.¹⁶⁴ The importance of several of these components in human nutrition is yet to be demonstrated However, recent work has definitely linked *nicotime* acid with pellagra, and *riboflavin* with certain mucous membrane changes. Other fractions of importance to the nutrition of laboratory animals are a filtrate (probably pantothlenic acid according to Jukes and Woolley, *ct al*), and vitamins B₃, B₄, B₅, and B₆.

Anemia — The relationship between the B₂ complex and anemias of the macrocytic type has been extensively studied. This relationship is demonstrated in pernicious anemia, sprue, and pellagra Rhoads¹⁶⁸ and others have recently summarized this information. Interesting data has been published by Wintrobe¹⁶⁹ showing that autolized yeast in doses of

15 to 30 grains (1 to 2 Gm.) per kilogram of body weight per day will produce a blood response in patients with pernicious anemia Liquid extracts of yeast were without effect. Brewer's yeast was more effective than baker's

Riboflavin — According to Dann, 164 riboflavin has been shown to be closely related to cell enzymes and aids in controlling oxidative processes. It cannot be synthesized by the body. Chemical synthesis was accomplished in 1934. In experimental rats, deficiency was found to retard growth and favor development of dandruff and cataracts Dogs develop a peculiar collapse associated with yellow patches in the liver due to fatty de-In humans, Sebrell and generation Butler¹⁶⁵ have produced evidence that "cheilitis" is due to riboflavin deficiency. This condition is characterized by redness, desquamation and ulceration at the mucocutaneous junction of the lips with fissures in the corners of the mouth. It is believed by some that the skin lesions of pellagra and cheilitis may be closely related although the lip lesions may not respond to nicotinic acid. Spies and the Vilters 166 reported that the skin lesions of pellagra receded more rapidly on the addition of riboflavin Sydenstricker, et al. 167 describe 5 cases of cheilitis which were benefited by the administration of riboflavin These authors used 3 to 60 mg of riboflavin daily. The parenteral route seemed more effective. The lesions were slow in healing and showed a marked tendency to relapse quickly on stopping therapy. Their patients were pellagrins

Dermatitis.—This is a frequent finding in B₂ deficiency in experimental animals. Dann (loc cit.) suggests a common dermatopic function in all fractions of B₂. Lack of 1 component may result in the breakdown of a molecule composed of all fractions. A large amount of any

1 factor might overcome deficiency of another by mass action. The most important fractions in this respect seem to be B_6 and the filtrate factor previously mentioned.

Vitamin B_6 —This fraction of the B complex has been chemically isolated and synthesized. Spies, et al, 173 reported 4 patients treated for pellagra and beriberi with synthetic materials who had continued symptoms consisting of nervousness, insomnia, irritability, abdominal pain, weakness and difficulty in walking Within 4 hours after subcutaneous administration of $\frac{3}{4}$ grain (50 mg.) of synthetic B_6 in salt solution, there was a dramatic response and within 24 hours the symptoms had disappeared.

Chemically, this material is a derivative of pyradine and is closely related to nicotinic acid. Birch¹⁷⁴ suggested that a possible physiologic function of this substance is the utilization of the unsaturated fatty acids

Nicotinic Acid—This substance has been shown to be a specific cure for most of the symptoms and signs of pellagra. Spies and his co-workers and others have done exhaustive studies in this field recently reviewed in publications by the former ^{170, 171}

In typical pellagra, one of the early signs is the characteristic glossitis, later followed by stomatitis, gingivitis, and pharyngitis Nausea, vomiting, ptyalism, and diarrhea may appear. Anorexia, abdominal distention, pain, and discomfort are common symptoms Dermal lesions may occur on any part of the skin but are commonest on the dorsa of the hands and feet, axillae, elbows, wrists, knees, beneath the breasts and in the perianal At first, the affected area is erythematous and may burn or itch severely Bullae and vesicles may develop Later, the color becomes darker and desquama-These lesions are usually tion begins

symmetrically distributed and sharply demarcated. Pigmentation usually follows healing. *Psychoses* are frequent and may consist of confusion, loss of memory, disorientation and confabulation. Peripheral nervous symptoms are often present and consist of burning, numbness, and tingling, and alteration of reflexes (polyneuritis).

Adequate dosage of nicotinic acid results in marked changes in all the above symptoms and signs within 24 to 72 hours, except those due to peripheral neuritis which requires additional vitamin B₁ (thiamin). The required dosage is variable but Spies (loc. cit.) suggests 7½ grains (500 mg.) daily divided into 34 grain (50 mg.) oral doses Smaller amounts may suffice. Parenterally, total daily dosage varies from $\frac{2}{3}$ to $\frac{1}{3}$ grains (40 to 80 mg.) in physiologic salt solution given intravenously The authors stress the importance of an adequate diet as soon as it can be tolerated. This program should include liberal amounts of lean meat, milk, and eggs. In the absence of such food, the use of $2\frac{1}{2}$ ounces (75) (m) of brewer's yeast daily is suggested as a supplement. In pellagrins whose diet cannot be appreciably improved, the authors advise continued administration of $\frac{3}{4}$ grain (50 mg) of nicotinic acid 10 times daily, thiamin chloride, 16 grain (10 mg) twice daily, and riboflavin, 112 gram (5 mg.) once daily Oral administration is preferred except in the severely ill.

Spies, et al (loc cit) explain the physiologic activity of these substances (thiamin hydrochloride, nicotinic acid and riboflavin) on the basis of their being components of important intracellular enzymes. The final information regarding the nature and functions of these enzymes is not yet at hand.

Since the original work on nicotinic acid, many synthetic compounds have

been tested for their effectiveness in treating pellagra. Spies and his co-workers¹⁷⁵ have reported experiments with 4 compounds closely related to nicotinic acid (pyridine carboxylic acids), none of which was very satisfactory. Two related compounds (pyrazine carboxylic acids) were found to be effective and did not produce the vasomotor symptoms sometimes seen with nicotinic acid.

Elvehjem¹⁸⁵ states that evidence has been found suggesting the possible importance of another factor in the B complex, factor W, in the treatment of pellagra. A more rapid response to nicotinic acid may be obtained by the addition of this material obtained from liver extract.

Vitamin C

Sources:

- 1 Citrous fruit, tomato and raw cabbage juice, strawberries, water cress, etc
- 2 Cevitamic acid

REQUIREMENTS:

Six hundred to 1200 international units (30 to 60 mg cevitamic acid).

SYMPIOMS AND SIGNS OF DEFICIENCY.

Scurvy Spongy bleeding gums, hemorrhagic tendencies, sore and swollen joints, delayed wound healing, increased capillary fragility, edema

CAUSATIVE FACTORS

- 1 Insufficient intake
- 2 Faulty absorption (achlorhydria, enteritis).
- 3 Increased demand (fever, infections)
- 4 Increased excretion (renal threshold)

Diagnosis .

- 1 History and physical examination
- 2 Urinary excretion with or without test
- 3 Blood cevitamic acid (normal 0.7 to 1.3 mg. per cent)
- 4 Capillary fragility
- 5 Intradermal test

TREATMENT

Thirty to 1000 mg per day by mouth or intravenously.

The primary function of vitamin C has to do with maintenance of normal

mtercellular cement substances of endothelial tissues. Daily requirements have been variously estimated at from 600 to 1200 international units (½ to 1 grain—30 to 60 mg.—cevitamic acid). Deficiency results in bleeding tendencies probably dependent upon increased capillary fragility. Severe deficiency causes the typical picture of scurvy with spongy bleeding gums, subperiosteal hemorrhages and edema. Delayed wound healing has been described.

Synthesis of ascorbic or cevitamic acid in 1933 has made possible extensive studies of its importance in various disease states, as well as studies of the various food sources. Spellberg and Keeton¹⁷⁷ summarize recent experimental work as indicating that: (1) Ascorbic acid is excreted in the urine in its reduced state in most persons. The amount of excretion depends upon intake and in normals it exceeds a minimum of 1/3 grain (20 mg.) in 24 hours. (2) The normal blood level of ascorbic acid is at least 07 to 09 mg. per cent. (3) Storage occurs in most body tissues. The degree of such storage is indicated by the result of saturation tests A normal person should excrete at least 30 per cent of a 91/4 grain (600 mg.) dose in 24 hours. After saturation of body tissues by large doses, 75 per cent of any test dose should be excreted in the urine Febrile conditions may alter these tests since there is often decreased excretion not dependent on decreased intake

These writers studied vitamin C metabolism in a variety of conditions. Previous work has shown that while patients with clinical scurvy have low blood and urine concentrations, the same levels may be found in persons without signs of scurvy. These authors found that studies of basal urinary excretion were unreliable probably because of varying degrees of saturation and vari-

able renal thresholds. Tests of degree of saturation are necessary for proper interpretation. For the diagnosis of scurvy these writers believe one must demonstrate a lowered renal threshold for ascorbic acid and extreme depletion of body stores with delayed saturation on large doses of vitamin C.

The value of vitamin C tolerance tests in hemorrhagic states is discussed. Occasionally the differentiation between purpura and scurvy is very difficult. Here the saturation test may be of value although it must be remembered that a patient with purpura may also be vitamin C deficient.

In hyperthyroidism there may be alteration in vitamin C metabolism resulting in disturbed saturation tests. Apparently the demand for this vitamin is greatly increased by the greater metabolic activity so that excretion of test doses is lowered even though blood levels become normal. Decreased excretion of test doses was also noted in cases with malignant tumors. In fact, this finding was so consistent that the authors suggest its use in diagnosis. In 3 cases with suggestive findings of carcinoma but with normal vitamin C tolerance tests, cancer was later disproved. In cases with carcinoma there was always less than 75 per cent excretion of test doses after saturation. In leukemia there is also increased utilization.

A study of peptic ulcer patients indicated that deficiency occurs after following the Sippy program for 3 weeks. This may be of importance in producing delayed healing and may favor hemorrhage. It was found that administration of alkalis lowered urinary excretion, possibly because of increased storage. No disturbance of vitamin C balance was found in association with hepatic cirrhosis.

A possible relation between vitamin C deficiency and failing vision was indicated by the studies of Bouton.¹⁷⁸ He determined 24-hour excretion, blood levels and response to a test dose in a group of employees and patients in a state hospital. Those with "aging eyes" were treated with ascorbic acid. Improvement was noted in 2 weeks in those without definite cataracts

The effect of vitamin C on bacterial toxins and various viruses has been noted by many. Jungeblut179 cites previous work showing in vitro neutralization of vaccinia virus, herpes virus, rabies virus, foot and mouth disease virus, tobacco mosaic virus, bacteriophage, diphtheria, tetanus, dysentery, staphylococcus and anaerobic bacterial toxins The effects of vitamin C in vivo in this connection have not been encouraging The author reports studies with the virus of anterior poliomyelitis Neutralization occurred in vitro but in monkevs the results were variable. After preparation with adequate vitamin C many monkeys escaped evidence of infection after intracerebral doses of virus.

Vitamin C has proved of value in treating lead poisoning, according to Holmes^{180, 181} and his co-workers was found that patients with chronic plumbism improved with addition of ascorbic acid. In test tube experiments it was found that vitamin C reacts with lead ions to form poorly ionized compounds which are less toxic than lead itself Thirty-four patients with chronic lead poisoning were treated with 1½ grains (100 mg) of ascorbic acid daily; half of this group also received calcium In the patients on vitamin C alone, improvement was noted both clinically and by laboratory tests These changes were more marked in this group than in those receiving calcium. It was found that patients with lead poisoning excrete less vitamin C than normals, and also that less lead was found in the urine of these patients receiving vitamin C treatment. The authors suggest that this is additional evidence that vitamin C combines with lead to form a poorly ionized salt. The decreased urinary excretion of lead in this treatment may be explained by increased fecal excretion resulting from increased hepatic excretion of lead in the bile, although evidence supporting this hypothesis is not offered.

Vitamin D

Sources .

- 1 Some fish, eggs, milk, meat products
- 2. Fish liver oils, viosterol

REQUIREMENTS

- 1. Infants—Three hundred to 400 international units per day
- 2. Adolescents—Three hundred international units per day
- 3 Adults-Uncertain

Lactation and Pregnancy—Eight hundred or more units

SYMPTOMS AND SIGNS OF DEFICIENCY

Rickets, infantile tetany, osteomalacia, dental caries

CAUSATIVE FACTORS

- 1 Insufficient intake
- 2 Increased metabolism (pregnancy)
- 3 Lack of absorption (biliary disease, celiac disease)

DIAGNOSIS

- 1 History and physical examination
- 2 Blood calcium, blood phosphate, serum phosphatase
- 3 X-rays of bones

TREATMENT

- 1 Cod liver oil 300 to 600 units (up to 50,000 in severe rickets)
- 2 Ergosterol 600 to 1000 units
- 3 Ultraviolet irradiation
- 4 Adequate calcium and phosphorus intake

This fat soluble vitamin is necessary for the absorption of calcium and phosphorus and their deposition as bone. In growing children the demand is undoubtedly greater than in adults except under unusual conditions. The minimal antirachitic requirements probably range between 300 and 1000 international units. For therapeutic purposes in infants, much larger doses have been recommended. Park¹⁸⁶ states that daily doses of 50,000 units may be given for rapid healing in advanced rickets.

The effect of large doses of vitamin D in arthritis has received considerable study. Steinberg¹⁸⁷ reports detailed studies on 40 cases given 200,000 to 500,000 units per day. Improvement was noted in about 50 per cent of 29 cases of atrophic arthritis and in about 30 per cent of 7 cases of hypertrophic arthritis. Determination of serum calcium showed a lowering of high levels and a raising of low levels by these large doses of vitamin D. There was no correlation between clinical results and blood calcium levels.

Vitamin E

Synthesis of this vitamin was reported in 1938 by Karrer. 188 Formerly wheat germ oil was the most potent source. In animals there is considerable evidence that deficiency results in premature separation of the placenta with abortion. To date the evidence in humans is meager, but Vogt-Miller, Shute and others 189 report marked success of vitamin E administration in cases of habitual abortion.

Vitamin K

Sources

- 1. Alfalfa, liver, fish meal, egg yolk, etc
- 2 Synthetic vitamin K, phthiocol

REQUIREMENTS

Unknown.

SYMPTOMS AND SIGNS OF DEFICIENCY

Hemorrhagic tendency, particularly jaundiced states

Decreased blood prothrombin

CAUSATIVE FACTORS:

 Faulty absorption due to lack of bile in intestines.

- 2. Insufficient intake.
- 3 Liver function ?

DIAGNOSIS

- 1. Determination of blood prothrombin.
- 2 Abnormal bleeding in jaundice

TREATMENT (Snell, et al):

- 1 Prophylaxis in jaundice—Two to 6 capsules of 200 mg, of alfalfa concentrate, 1 to 2 Gm bile salts
- 2. In bleeding or reduced prothrombin—One to 2 Gm alfalfa concentrate; 2 to 4 Gm bile salts, via duodenal tube if necessary
- 3. Intramuscular injection—Five to 10 mg synthetic vitamin K.

Since the original clinical reports of the value of vitamin K in hemorrhagic states associated with jaundice were made by Warner, et al, 190 and Butt, et al, 191 in 1938, there has been active investigation of this phenomenon. Snell and Butt 192 have recently reviewed the progress of these studies

Chemistry—Almquist and Klose, 193 and Dam, et al, 194 have produced a purified oil which they believed to be practically pure vitamin K. Other closely related substances have been obtained from alfalfa and putrefied fish oil195 and from cultures of the Mycrobacterium tuberculosis 196 This latter substance, phthiocol, has been synthesized and found to be effective. From this information, these and other workers197, 198 have evolved the following structural formula for vitamin K 2 methyl-3 phytyl-1-4 naphtha quinone Synthesis of this compound was reported by the latter writers

Determination of Deficiency—Clinical determination of vitamin K deficiencies depends upon the measurement of prothrombin. The method of Quick is generally accepted for clinical purposes. Smith, *ct al*, ¹⁹⁹ have suggested a simpler technic which in their hands was acceptable. This consists of comparing the clotting time of normal blood to that

of the patient after adding thromboplastin to each. The result is expressed in the percentage of the normal clotting time.

Causes of Deficiency—Prothrombin deficiency (hypoprothrombinemia) which is apparently dependent upon an inadequate supply of vitamin K may occur in a variety of conditions. Snell and Butt¹⁹² have summarized this data as follows: (1) Inadequate dietary intake; (2) newborn infants, (3) inadequate intestinal absorption due to (a) lack of bile due to faulty secretion, (b) biliary obstruction, (c) intestinal lesions such as obstruction and short-circuiting operations, (4) hepatic injury. Experimental work has shown that liver injury or removal results in lowered prothrombin levels. If the liver function is sufficiently impaired, administration of vitamin K and bile salts may not result in improvement, indicating that the liver is necessary in the formation of prothrombin.

Administration—The amount of vitamin K required in any given case has not been determined Smith, et al, 199 point out that some of the vitamin is manufactured by intestinal bacteria and some is normally present in the diet The feeding of bile salts alone may restore the blood levels to normal in some cases. More rapid recovery is obtained by giving the vitamin in some form These writers advise the daily use of extract from 10 to $13\frac{1}{3}$ ounces (300 to 400 Gm) of alfalfa meal and at least an ounce (30 Gm) of bile or its equivalent in bile salts. On this program a maximal response should be obtained in from 3 to 5 days (Commercial vitamin K preparations include "Klotogen," Abbott Laboratories, North Chicago, Ill., and "Cerophyl," Cerophyl Laboratories, Kansas City, Mo.) Butt, et al, 200 advise the preoperative administration of 2 to 6 capsules containing about 3 grains

(200 mg.) of alfalfa concentrate and 15 to 60 grains (1 to 4 Gm.) of bile salts daily for 2 to 5 days. In patients showing marked reduction in prothrombin larger doses are advisable. Administration by duodenal or common duct T tube may be necessary. In these cases a solution is made of $\frac{1}{2}$ to 1 dram (2 to 4 Gm.) of bile salts in 8 to 16 ounces (250 to 500 cc.) of warm physiologic salt solution or tap water. To this is added 15 to 30 grains (1 to 2 Gm.) of alfalfa concentrate and the solution administered slowly through the tube. One such dose, as a rule, will restore the prothrombin level to normal, although it may have to be repeated. Stewart and Rourke²⁰² use a mixture consisting of 7 grains (045 Gm) sodium glycocholate, 7 grains (045 Gm.) sodium taurocho*late* and $1\frac{1}{2}$ grains (0.1 Gm.) of extract obtained from 6\(\frac{1}{3}\) ounces (200 Gm) fresh spinach. The daily dose used by these writers was 18 grains (1.2 Gm.) of this mixture. They also advise the use of $13\frac{1}{3}$ ounces (400 to 600 Gm) of carbohydrate daily, either by mouth or vein.

Attempts have been made to administer vitamin K by parenteral routes Snell, *et al*, ¹⁹² report results of their own and others following intramuscular injection. As a rule the response to this procedure is slow and these writers feel that peroral administration is still preferable if possible.

Intravenous injection of synthetic compounds having antihemorrhagic action has been reported by several workers. Smith, et al, 199 report 1 case treated by a 02 per cent solution of phthiocol intravenously and Butt, et al, 201 treated 9 patients with intravenous injections of a solution of synthetic phthiocol. Neither report notes any untoward effects. In all instances the prothrombin level was increased by the procedure. Snell 192 reports 10 patients

treated with another synthetic compound, 1. 4-dehydroxy-2-methyl-3-naphthaldehyde (supplied by Dr. E. A. Doisy of St. Louis). Intravenous injection of 5 to 10 mg. of this preparation reduced prothrombin times and was without untoward reactions.

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HEMATOLOGY

By WILLIAM DAMESHEK, M.D.

BLOOD-FORMING ORGANS

Schulten has stated that study of the bone marrow at biopsy may be considered as the "hochschule" of hematological observation of the peripheral blood In other words, as the Reviewer has frequently stated, the blood simply reflects the reactions of the blood-forming organs, principally the marrow. In many cases, it reflects poorly or madequately the conditions within the marrow cavi-Whether this is the case or not, it becomes of definite value to understand what is "behind" the blood picture, and this the examination of the marrow helps us to do.

Study of the marrow has been greatly facilitated in recent years by sternal puncture with use of a needle similar to that used in lumbar puncture. The technic is simple, readily mastered, and the preparations obtained are excellent, providing certain precautions are observed The needle must be introduced into the marrow cavity (a sensation of "give" is felt); the marrow "juice" should come up into the syringe freely with very little suction, only a very small amount of material should be sucked up (about 0.5 cc.) to avoid too much dilution with blood; smears should be made carefully and gently on specially cleaned slides and stained with Wright-Giemsa

Proper identification of cells and interpretation of marrow pictures may both be mastered by assiduous practice, provided the observer realizes the limitations of the method From the diagnostic standpoint, sternal puncture is especially valuable in cases with "pancytopenia" *i e*, those with anemia, leukopenia, thrombocytopenia (representing a reduction in the 3 marrow elements) In such cases, which are often diagnostic puzzles, the blood picture may be identical though the marrow may be the seat of highly dissimilar conditions Aplasia; Gaucher's infiltration, lymphosarcoma and leukemia. Of these the commonest by far m our series has been leukemia (aleukemic). P Vogel and F. A Bassen¹ report their experiences with this procedure in infants and children used a half-inch, 18-gauge lumbar puncture needle for children over 1 year of age and a 20-gauge, one-quarter inch needle for infants under 1 year; no anesthesia was necessary. The puncture was

useful as a diagnostic aid in cases of atypical anemia, leukemia, and in making a positive diagnosis in cases of Gaucher's disease and malignancy.

Physiologic relationships between the blood and the bone marrow are of interest even when there is no question of diagnosis. An interesting study is that of M. Ungricht² who studied the relationships of the reticulocytes of blood and bone marrow. The marrow reticulocytes outnumbered those of the blood in all normal and abnormal conditions excepting only that of congenital hemolytic jaundice. Interpretations relating to the delivery and maturation of the reticulocyte are made.

BLOOD CELLS

Red Blood Cells

The use of the blood groups for the determination of paternity is receiving increasing attention By using the ordinary blood groups - O, A, B, AB paternity can be disproved in only a small percentage of cases With the development of knowledge regarding the M and N blood types (Landsteiner and Levine), great impetus was given to this form of testing and it is now possible by the combined use of both the ordinary and the M and N types, to disprove paternity in 33 to 40 per cent of all cases The most difficult part of the procedure is the preparation of anti-M and anti-N testing fluids. This subject has been thoroughly covered by I. Davidsohn and I. Rosenfeld,3 specific directions for proper preparation of serum being given It is hoped that more States besides New York and Wisconsin will pass suitable laws making blood grouping tests obligatory in cases of doubtful paternity.

An interesting method for the study of the lifetime of the erythrocyte is pre-

sented by H. J. N. Dekkers⁴ who transfused recipients with compatible blood but with different M and N groups. By performing "direct-differential-agglutination tests" with anti-M and anti-N test sera, Dekkers showed that the transfused red cells gradually disappeared in about 2 to 3 months.

A. L. Florman and M. M. Wintrobe⁵ in describing 3 families with elliptical red cells point out that these cells are commonly found in anemic, and to some extent in normal individuals. They appear to be without definite significance.

E. H. Falconer⁶ studied the clinical significance of punctate basophilia in the erythrocyte. Of chief importance was the setting up of standards for the appearance of stippled red cells in normal individuals, those with miscellaneous conditions, and those with lead poisoning. Jenner-Giemsa stain was used and about 5000 red cells observed for stippling. The normal group had a mean punctate basophilia of 92 cells per million red cells. The miscellaneous group averaged 363 per million red cells. In various types of anemia not due to lead the mean stippled count was from 2000 to 27,000. In 8 workers exposed to lead but free of symptoms the average stippled count was 2100 per million red cells. Thus, stippling of the red cells, although common in lead poisoning and often diagnostic, is not pathognomonic of this condition but may occur in various states, particularly those associated with anemia

The sedimentation rate continues to receive much attention. There is still some discussion regarding the type of test to use. Ham has compared them carefully and concludes that the Rourke-Ernstene test using heparin and correcting for cell volume is the most accurate. However, most writers agree that the simpler Westergren test using citrate is adequate enough for clinical work.

Thus A. Hambleton and R. A. Christianson⁷ state "Alleged improvements Westergren sedimentation upon the method have been presented which appear theoretically correct, eg, correction for cell volume, the use of heparin in place of citrate, and graphic methods of recording the results Instead of making the test more valuable, these changes have the reverse effect, either by leading to results of less clinical value, or by making the test more tedious to perform or less clear to interpret without increasing its clinical value. Hence it is recommended that the Westergren method, by reason of its simplicity, reliability and priority, should be adopted as the standard method of performing the sedimentation test" N. H. Schuster8 comes to the same conclusions, although she concedes that for special cases and research work the blood count may be adjusted to a standard concentration. J. W. Cutler, F. R. Park and B S. Herr⁹ pointed out the great importance of changes in the serum upon the rate of sedimentation A "fast" serum from a severe infection results in quick aggregation of rouleaux and a rapid sedimentation even when normal red cells are substituted in the test. Serum changes are far more important, they believe, than concentration of red blood cells Henry Bunting 10 has shown that the tendency to form rouleaux is greatly retarded in sickle-cell anenna with resultant great slowing of the sedimentation rate. The correlation of the sedimentation rate with blood fibringen which has been stressed by Cilligan has recently been criticized by M. W. Ropes, Elsie Rossmeisl¹¹ and Walter Bauer, who noted many exceptions to this correlation.

The various devices for estimating the dimensions of the normal and abnormal red cell are by now well known and coming into increasingly common usage.

These are the mean cell diameter, mean cell volume, mean cell thickness, mean corpuscular hemoglobin concentration. etc. Of these, the mean corpuscular volume has come into general use in the differentiation between normocytic, microcytic, and macrocytic anemia means of the Heller and Paul¹¹² oxalate mixture, blood is prevented from clotting and centrifuged to complete packing in Wintrobe hematocrit tubes. The hematocrit reading multiplied by 10 and divided by the red cell count in millions gives the mean corpuscular volume (M C V.) of the erythrocytes in cubic micra A M. C. V. of 84 to 94 (100) is normocytic, below 80 is microcytic; above 100 in macrocytic. K. Kato¹² has created an ingenious triaxial correlation chart which correlates the color index. the volume index, and the saturation index With use of this chart, it is possible, Kato states, to make "an accurate hematologic classification of all types of anemia, so essential a foundation for rational therapy" In addition, Kato gives simplified equations for calculations of volume and saturation indices The chief value of the various indices. aside from the intellectual diversion they might give, rests in the assistance they give for the therapy of anemia (q v)In infants, where venous blood is so difficult to obtain, the use of a "combination microhemopipette" has been advocated by K Kato¹² for the determination of hemoglobin, hematocrit, sedimentation rate, fragility test, as well as for the accurate measurement for other purposes of small quantities of blood.

Cyanosis of Sulfanilamide Therapy—A great deal of discussion has occurred regarding the character of the cyanosis which develops so commonly during sulfanilamide therapy. This was carefully studied by J. S. Harris and H. O. Michel ¹³ Methemoglobin, in

quantities demonstrable by the hand spectroscope (5 per cent or over), was found in the red cells of 58 per cent of 476 patients; sulfhemoglobin in 7.8 per cent. The extent of methemoglobinemia was found to correlate with the blood sulfanilamide concentration. Individual variation in methemoglobinemia might be influenced by various factors inherent in the body; it was commoner in the young. The postulation was made that an active substance which was produced in the course of sulfanilamide metabolism caused the production of methemoglobin and sulfhemoglobin

This theory was subjected to investigation by J. S. Harris 14 Animal tissues were incubated with sulfanilamide in the Sulfanılamıde presence of hemoglobin itself failed to result in the development of methemoglobin, but in the presence of animal tissue, another substance was formed which caused the development of the inactive pigment. David Campbell and T. N. Morgan¹⁵ concluded that the cyanosis of sulfanilamide and sulfapyridine was invariably due to the presence of either met- or sulfhemoglobin Methylene blue was found to be effective in causing the rapid disappearance of the cyanosis by converting the methemoglobin to hemoglobin. The methylene blue was given either intramuscularly (6 grams -400 mg), intravenously $(2\frac{1}{2})$ grains--150 mg), or by mouth (15 erams—1 Gm)

White Blood Cells

In a series of papers, E E Osgood and collaborators 16 discuss the total, differential and absolute leukocyte counts and sedimentation rates of (1) healthy children 4 to 7 years of age, (2) healthy children 8 to 14 years of age, (3) healthy adolescents 15 to 18 years of age, (4) healthy persons 19 years and over In the adult group, it was found that the

proportion of lymphocytes was higher and that of the polymorphonuclears lower than in textbook figures. The development of normal standards is necessary in the study of acute infections, just as a thorough knowledge of the blood in acute infections is necessary before the blood pictures from leukemoid and leukemia reactions can be appraised.

The blood picture and sedimentation rate were studied in low grade chronic illness by M. H. Slikes.¹⁷ Most of the patients were ambulant. One-half had chronic sinusitis and the rest had such abnormalities as nasal congestion, postnasal discharge, etc. Such other conditions as chronic bronchitis, colitis, prostatitis, "rheumatism," etc., were present. The immature polymorphonuclear cells (in this study classed as "nonfilament cells") were increased in practically all cases; as symptoms increased the ratio of nonfilament to filament cells increased. More than 80 per cent of the sedimentation rates were abnormal. It was shown that the blood smear examination was a more sensitive indicator of the presence of disease than the sedimentation rate, although the latter, because of its lack of sensitivity, might be more significant

M W Brachen¹⁸ studied the prognostic significance of the eosinophils in pneumonia Early in the disease, if severe, the eosinophils are absent; the appearance of eosinophils may precede clinical improvement or other hematologic evidence

The laboratory diagnosis of infectious mononucleosis is discussed by A. G. Foord and E. M. Butt ¹⁹ The Reviewer emphatically agrees with these writers in their statement that only a small proportion of the actual number of cases which occur are properly diagnosed. Perhaps this is not of outstanding importance, since all cases recover, but from the

standpoint of diagnosis of continued fever, leukemia, and abdominal pain, it is essential to know the disease and make the diagnosis. The condition is most often seen by the general practitioner who has the opportunity of bringing it to light. Generalized adenopathy, splenomegaly, a characteristic blood picture, and a serum test (the heterophile agglutination test) should all be sufficient to make the diagnosis. The peculiar, abnormal lymphocytes of the disease are well described by Foord and Butt, who also give an extended discussion of the sheep-cell agglutination test. tests are usually found as early as the fifth day, and a normal titer is reached, according to Davidsohn in an average of 119 days. Clinical recovery is rapid a matter usually of 2 to 4 weeks; complete hematologic recovery may take 60 to 90 days; complete serologic recovery is slowest.

Lymphoblasts, the most primitive lymphoid cells, are occasionally seen in the disease, although usually the blood is more abnormal and heterogeneous than primitive H Bowcock²⁰ reports the presence of mitotic blasts in 3 cases

The Lymphocyte—The function of the lymphocyte has for many years eluded numerous investigators. In a very interesting study A R Rich, M. R. Lewis and M. M. Wintrobe²¹ effectively showed by supravital motion-picture studies that the large cell of acute splenic tumor and of the regional lymphadenopathy of acute infections was an early or enlarged lymphocytic cell and not a monocyte or histocyte They pointed out that enlargement of spleen or lymph nodes was frequently nonspecific and noninfectious (allergy, horse serum, etc.). Because of the great lymphocytic hyperplasia, it was suggested that lymphocytes might have something to do with the formation of antibodies to foreign protein.

Agranulocytosis - The cases of agranulocytosis reported during the past year deal mostly with reactions to sulfanilamide and sulfapyridine. This complication appears not infrequently. A definite leukopenia of 4000 or under, particularly with sulfapyridine, should be the signal for discontinuance of the drug. When complete agranulocytosis occurs, the prognosis is exceedingly grave. I. L. Cutler and E. J. Crane²² report a recovered case following the use of transfusions and daily injections of $\frac{2}{3}$ ounce (20 cc.) of pentnucleotide. A case occurring after sulfapyridine administration was treated by M. E. Sutherland23 with transfusions; also with recovery One of the transfusions was preceded by the induction of leukocytosis in the donor by the intramuscular injection of 30 minims (2 cc) of veterinary nuclein, during the period of dropping leukocyte count, the administration of both pentnucleotide and liver extract was without effect V B Dolgopol and H M Hobart²⁴ report 2 cases of granulocytopenia and 3 of definite leukopenia which occurred in a relatively small series of cases of pertussis and pneumonia treated with sulfapyridine. There was I death, associated with the development of aplastic anemia. The possibility is suggested that the large dosage of drug used in these cases might have been at least partly responsible N. Rosenthal and P. Vogel²⁵ reported 3 cases of granulocytopenia in children following the administration of sulfapyridine In the first case, which recovered, the monocyte percentage was 30 Transfusions and liver extract were given. The other 2 cases died. Rosenthal and Vogel state

^{*}Ten cc of whole boiled milk intramuscularly will also result in a well-marked leukocytosis in about 1 to 2 hours

that it is important to follow the bone marrow (sternal puncture) as well as the blood picture in children who are receiving sulfapyridine for a prolonged or intermittent period. A definite reduction in the cellular content of the marrow should call for caution in the further use of the drug.

It has been the Reviewer's experience that the most severe reactions have occurred in those cases in which for some reason the drug is discontinued for a period and then resumed. During the first administration, it is possible that the body becomes sensitized to the drug with resultant "shock reaction" on the part of the marrow on readministration and agranulocytosis. It has become pretty well established that agranulocytosis represents a sensitization phenomenon on the part of the bone-marrow leukocytes to various chemicals, particularly those containing the benzene ring It is also possible that very large dosage of various drugs might of themselves, in a nonsensitized person, result in a hypoplasia of the marrow leukocytes with resultant granulocytopenia. This is borne out in certain animal experiments of E. M. Butt, A. M. Hoffman and S. N. Soll 26 Dogs given large doses of amidopyrine over a long period of time developed a toxic hypoplasia of the marrow with leukopenia. The importance of discontinuance of the drug on the appearance of definite leukopenia is ob-Vious Daily leukocyte counts indicated.

Leukemoid reactions are occasionally seen, and the possibility exists, as Rohr²⁷ has pointed out, that in certain instances leukemia may develop. One wonders whether individuals who have become sensitized to these drugs might not on some future occasion develop a leukocytic disease when the same or simi-

lar drug is administered for another infection.

Treatment—The treatment of agranulocytosis is generally conceded to be very unsatisfactory. Transfusions, liver extract, yellow bone-marrow extract, pentose nucleotides, adenine sulfate, x-ray therapy—all have their adherents but none has been definitely shown to be specific. H. Jackson, Jr., and T. J. G. Tighe²⁸ analyzed 396 cases recorded in the literature since 1933. The mortality in 75 untreated cases was 78 per cent. Neither transfusions nor x-ray therapy appeared to alter the mortality rate. There was an equivocal reduction (to 62 per cent) in 26 cases treated with adequate amounts of liver extract. They found that treatment with yellow bonemarrow extract, leukocytic cream or adenine sulfate had not been widely enough reported to permit any accurate conclusions as to their worth; however, these measures were considered to be worthy of further trial. The mortality in 85 cases treated with pentnucleotide was 35 per cent It is suggested that doses of at least $1\frac{1}{3}$ ounces (40 cc.) per day be given

The results of Jackson and Tighe are not in agreement with those of various hematologists throughout the country with whom the Reviewer has discussed the subject. These men have all been disappointed with the various forms of recommended therapy and, like the RE-VIEWER, believe that the various measures used are of only questionable value Some years ago, the REVIEWER believed. on the basis of his results with the adenine sulfate and pentinucleotide, that if adequate doses of these drugs were given early in the disease a beneficial result could be expected in about two-thirds of the cases. The death of all but 2 of 15 more recent cases treated in the same vigorous manner has led to a more pessi-

mistic attitude. It is now thought that if the bone marrow is not too severely damaged, recovery may ensue spontaneously; however, if the leukocytic tissue is seriously impaired, the various therapeutic measures are justified chiefly as gestures, but their ultimate value is questionable.

Platelets

The platelet count has frequently been stressed by the Reviewer as a means of obtaining, with the erythrocyte and leukocyte counts, a complete index of bone-marrow activity. F. J. Pohle²⁹ studied the platelet count in relation to the menstrual cycle in normal women. He used a direct method which involved shaking the red counting pipette in an automatic shaker for 5 minutes (It is probable that many platelets become broken up during this procedure) The average platelet count with this method was 265,000, which is somewhat less than half that obtained with the indirect methods of I Olef³⁰ and the Reviewer 31 Venous platelet counts were 15 per cent higher than those obtained from capillary blood. More than 1000 platelet counts were made on 13 normal, menstruating women It was found that the platelet count declined progressively 2 weeks before the catamenia and that the lowest platelet count was present on the day of onset of the menses, following which there was a rapid rise. It is not clear from Figure 3 in this paper whether the marked increase in platelets took place on the first or second day of the menstrual cycle. (The Reviewer found a marked increase at the beginning of the menses.) There can be no doubt, however, of the marked cyclical relationship of the platelet count to the menstrual cycle, this may be related to the sex hormones P. Lee and B. N. Erickson³² studied the number and disintegration rates of platelets in normal women and men, and in cases of hemophilia and thrombocytopenic purpura. Olef's methods were used. It was found that the platelets of hemophiliacs disintegrated less rapidly than those of normal individuals (this contention has been disproved by several workers) and that patients with thrombopenic purpura were hypersensitive to intradermally injected platelet suspensions. The latter results are interesting but require confirmation. J. Arneth³³ studied the platelet count in old age and found essentially normal values.

ANEMIA

Pernicious Anemia

W. Jacobson³⁴ studied the argentaffine cells of the stomach in normals and individuals dying of pernicious anemia. These cells were found to correspond in their location to those of the Brunner glands in the pyloric and cardiac regions of the stomach, in the duodenum and frequently in other parts of the small intestine. In 12 cases of pernicious anemia, the argentaffine cells were either completely or almost completely absent. These findings must be compared with those of E Meulengracht35 who had also concluded from previous studies that the cells in the above regions were concerned with the elaboration of "intrinsic substance" and were therefore involved in pernicious anemia. Surprisingly enough, however, the areas actually found involved in cases of pernicious anemia were those about the fundus, whereas the pyloric gland or Brunner regions were entirely normal Meulengracht was forced therefore to postulate a functional insufficiency of the Brunner glands due perhaps to a lack of "pacemaker" in the fundic glands.

M. M. Wintrobe, M. Samter, and H. Lisco³⁶ produced a close analogue of pernicious anemia in pigs by feeding them shortly after birth with a diet deficient in certain factors of the Bo complex. Complete hematological data and gastric analyses were obtained. Occasionally, sternal bone-marrow biopsies were performed. Anemia did not occur if sufficient amounts of yeast were given, but in the absence of yeast, anemia with macrocytes and nucleated erythrocytes occurred. There was no effect with the administration of mcotinic acid, riboflavin, or vitamin B₁, but reticulocytosis and either partial or complete relief of the anemia occurred with the administration of yeast Liver extract was without value. The bone marrow became hyperplastic and neurological changes developed

These experiments are confirmatory of the theory that pernicious anemia is a deficiency disease, perhaps concerned with a long-standing dietary deficiency, either as such, or conditioned by an abnormality of the gastrointestinal tract. A clinical report along the same lines is that of G. Alsted³⁷ on "Exogenous pernicious anemia" This report deals with the case of a man who, because of constipation, radically modified his diet, eating for 7 years nothing but white bread, butter, porridge, cream, and 1 egg daily The findings were those of pernicious anemia but the gastric analysis revealed a small amount of free hydrochloric acid after histamine injection. Alsted treated him with a diet high in foods containing the "extrinsic factor" with an excellent result and with an increase in the gastric hydrochloric acid Most investigators have assumed that the hydrochloric acid and "intrinsic factor" or enzyme of Castle are reduced in pernicious anemia because of atrophy of the respective glands involved That a secretory depressant may be present has not been greatly discussed. A. Brunschweig, J. V. Prohaska, T. H. Clark, and E. Kandel³⁸ injected the gastric juice of cases of pernicious anemia in dogs with gastric pouches. There was a marked transitory depression of the pouch secretion and achlorhydria in 89 per cent of the samples, whereas in the controls, a depressant activity took place in only 18 per cent. The possibility that a gastric secretory inhibitor is present in pernicious anemia is discussed.

Megaloblast—M. C. G. Israëls³⁹ discusses the pathological significance of the megaloblast, first applied by Ehrlich to a large nucleated red cell found in the blood and bone marrow of patients with pernicious anemia. Israels confirms the findings of W. Dameshek and E. H. Valentine⁴⁰ on the bone marrow in pernicious anemia and with these workers concludes that there are 2 types of erythropoiesis: a megaloblastic, seen in liver-extract deficiency states and a normoblastic, seen in all other conditions. Israels states that for future clarity it is important "that the term megaloblast should be restricted to the cells to which it has been applied here and by Dameshek and Valentine, that its use as a term for what are here called progrythroblasts and hemocytoblasts should be discontinued . . . "

Pathogenesis — J G Gibson, Jr.⁴¹ studied the changes in blood volume in pernicious anemia before, during, and after treatment with liver extract In relapse, there was a "hydrenic hypovelemia" which returned to normal levels with return of the blood counts to normal. R. Schindler and A. M. Serby⁴² report on 34 gastroscopic observations of 23 patients with pernicious anemia All untreated patients presented superficial gastritis, atrophic gastritis, or patchy atrophy. In 12 cases after treat-

ment there was a return of either the entire gastric mucosa or the mucosa of the antrum to normal; in 5 cases, there was no improvement. Schindler and Serby postulate that 2 separate disorders are present in pernicious anemia (1) a primary disorder of the cells producing the antianemic factor and (2) a gastritis which may or may not heal when the deficiency state is eliminated (cf. the observations of Meulengracht above). The secondary gastritis is usually combined with a similar disorder of the tongue and intestine Mucosal polyps are common.

Treatment—C. C Sturgis⁴³ reports on the therapy of approximately 1000 patients treated by various methods of liver and stomach therapy between the years 1927 and 1938 Approximately 10 per cent died either of complications incident to extensive involvement of the nervous system or of incidental and unrelated diseases None of the patients died of anemia per se Sturgis takes up the possibility that the neurological lesions may be due to a different deficiency than the hematological, and that in the future a specific substance may be discovered which is more effective than liver extract for these often intractable symptoms; this involves keeping the patient's red cell count at a sufficiently high level

In Denmark, Meulengracht (Lecture before Wisconsin Hematological Conference, August, 1939) has found that this can be done with oral therapy, using "pylorin"—a pyloric gland preparation—which is apparently of greater potency than the American ventriculin. He found that intramuscular therapy was too expensive for most Danish individuals and of no greater potency than pylorin. All authorities agree that one must give sufficient therapy and that too much treatment does no harm. Sturgis, who

has had considerable experience with ventriculin, states that the most efficient treatment of the disease at present is the intramuscular administration of liver extract. The Reviewer uses only parenteral therapy in the neurological cases and often without reference to the red cell count. Even at a normal red count. neurological phenomena may still be present and may well respond to very intensive parenteral therapy. The posterior column disturbances, ataxia, in-co-ordination, diminution in knee jerks and in vibration sense, may respond wholly or in part to continued and effective treatment; the lateral column disturbances are less effectively treated. In our hands, highly concentrated and refined liver extracts have been highly effective in the therapy of these cases This appears to rule out the possibility that cruder extracts are essential because of their content of "other factors"

Simpson Memorial Institute have worked out standards for maximum reticulocyte percentage, average reticulocyte count, and red cell increase after liver-extract therapy 44 The maximum reticulocyte count depends directly upon the initial red cell count the lower the count, the higher the reticulocytosis, this may be expressed by the formula Reticulocyte 82-22 Erythrocyte count The 1+05 Erythrocyte count. chart dealing with the red cell count increase brings out the interesting point that within 8 weeks the erythrocyte count will be normal, at whatever point the initial red count begins In other words, the lower the red count, the more rapid is the red cell increase.

Members of the Ann Arbor group at

Macrocytic Anemia, Other Than Pernicious Anemia

Anemia with high color index, average red cell size above 7.5 micra, and mean

corpuscular volume of at least 100 cu. micra is usually due to liver-extract deficiency (pernicious anemia). It may, however, be due to other causes, gastrointestinal or otherwise. C. C. Sturgis and S. M Goldhamer⁴⁵ in a very interesting article, describe various cases of macrocytic anemia with lesions of the stomach. the intestinal tract, and the liver. The reason for the development of macrocytic anemia in severe liver disease is not very well defined. Although the commonest explanation given is that a greatly diseased liver results in deficient storage of liver extract with resultant diminished quantity of material going to the marrow, this may be incorrect since the marrow in several cases studied by the Reviewer was not megaloblastic (i.c., liver-extract deficient).

Cases of liver-extract deficiency, whether "primary" or definitely secondary in type, respond readily to liverextract therapy, but most cases of severe hepatic disease with macrocytic anemia respond little if at all to liver extract. Macrocytic anemia may also occur in the "Sprue Syndrome" so well described by A M Snell 46 In 20 of 32 cases, the symptoms and signs were indistinguishable from those of tropical sprue; these patients responded in a specific manner to liver extract. The remaining 12 cases presented various metabolic and nutritional disturbances, including tetany, osteoporosis, hypoproteinemia, and various vitamin deficiencies. This condition is ordinarily described as idiopathic steatorrhea (Gee's disease). The response to liver extract in the latter cases was rather unsatisfactory

Cehac disease of children is also probably a similar condition at a different age and usually responds well to liver extract or whole liver A deficiency in vitamin B complex may also lead to macrocytic anemia; this is usually best

treated with dilute liver extract, whole liver, or yeast concentrate tablets. The latter materials contain all the constituents of the very important vitamin B complex: vitamin B_1 ; nicotinic acid, riboflavin, the rat anti-dermatitis factor (vitamin B_6), the W. factor, and probably other undefined factors as well. An experimental B_6 deficiency anemia has been described by P. J. Fouts, O. M. Helmer and S. Lepkovsky 47

The Reviewer has recently 48 studied vitamin B₂ deficiency in pigeons; a deficiency state associated with anemia and a hyperplastic marrow develops Therapy with nicotinic acid, riboflavin, and vitamin B6 were without effect but dilute liver extract and yeast were dramatically effective. The exact deficient factor at fault was not defined although this might have had some relation to the chick antidermatitis factor. It is well to remember that if one desires to give large doses of the entire vitamin B₂ complex (everything but B₁), this is accomplished either by giving yeast concentrate tablets orally (9 to 15 daily), or by administering intramuscular injections of a dilute liver extract.

Macrocytic anemia is not always due to deficiency disease, but may be due to hypoplasia or complete aplasia of the marrow, to chronic nephritis, to leukemia or to various conditions associated with invasion of the marrow cavity ("myeolophisic anemia"). In these conditions, there is almost always leukopenia and thrombocytopenia ("pancytopenia") and a complete lack of response to liver extract. Sternal puncture is frequently of help in clearing up the diagnosis of these doubtful cases

Iron Deficiency Anemia

II W. Josephs⁴⁹ studied the iron metabolism in infancy during well-controlled iron balance experiments. During

the first 3 months of life there was a slight tendency to a negative iron balance (loss of iron from the body); a positive balance was established later. Approximately 60 per cent of the food iron was absorbed; during infections and in vitamin D deficiency, there was a slightly diminished retention of iron. In anemia, iron was retained in greater than average amount; this pointed to the possibility that the tissues might be unusually "avid" for iron. It is possible that certain forms of iron are more "available" than others: that of vegetables and fruits may be relatively "unavailable": that of cereals more "available."

In another companion paper, Josephs⁵⁰ studied the retention and utilization of medicinal iron. Iron not only supplies a deficiency but appears to have a "stimulating" or "regulatory" function. Josephs believes that the iron within the body in hypochromic or nutritional anemia (of infancy) becomes for some reason unavailable; medicinal iron is, however. readily available Copper may have an effect on the total utilization of iron The iron deficiency anemia of infancy is rarely due, Josephs believes, either to hemoglobin loss or deficient dietary iron, but rather to rapid growth of the body and to other unexplained factors J. H. Vaughan and M. F. Saifi⁵¹ studied the hemoglobin metabolism in chronic infections By studies of the fecal urobilinogen and the relationship of this figure to the total circulating hemoglobin, it was determined that blood destruction was not increased. An increased excretion in both coproporphyrm I and III suggested a disturbance of hemoglobin synthesis with resultant anemia. The application of the newer methods of studying the physiology of the hemoglobin metabolism is of great interest and it is

chiefly for this reason the paper deserves a careful reading.

P. F. Hahn, W. F. Bale, E. O. Lawrence, and G. H. Whipple⁵² describe the results of studies made with radioactive iron in anemic dogs. Radioactive iron is "marked" iron and thus readily lends itself to the study of where iron goes to and how it is transported. In the normal dog, iron is absorbed in only negligible amounts, but in the anemic animal it is promptly assimilated Absorption takes place almost entirely by way of the mucosa of the small intestine whence the iron is transported in the plasma Within a few hours, in the anemic dog, some of the absorbed iron is found in the red cells of the blood The reticuloendothelial cells of the spleen and marrow take up large quantities of iron which acts as a reserve store of readily utilizable iron. C. V Moore, W. R Arrowsmith, V. Mınnick. and J Welch⁵³ continue their studies in iron transportation and metabolism in which the normal fluctuations of serum and "easily split-off" blood iron, and the absorption of iron from the gastrointestinal tract are discussed. The study of serum or plasma from is of importance because serial observations give an inkling as to the rapidity of transportation and absorption of ingested iron Moore and his collaborators present a large number of observations in experimental animals and on clinical material together with many illustrative charts. The serum iron absorption curves were higher following the ingestion of ferrous than of ferric salts; this was particularly true of the water soluble, highly ionized ferrous salts. Differences in gastric acidity exerted no measurable effect on serum iron absorption curves Ingested (food) iron is ordinarily acted upon by the free hydrochloric acid of the gastric juice to dissolve and ionize iron. In the duodenum, certain reducing agents probably reduce iron from the ferric to the ferrous form, in which form it is absorbed from the intestine, largely in the upper part of the small intestine. Iron thence passes directly into the blood plasma for transport to various tissues. According to A. Zih⁵⁴ the regeneration of red blood cells in the hemorrhagic anemia of guinea pigs is materially increased by the daily administration of ½60 grain (1 mg.) of bilirubin.

W. R. Kennedy⁵⁵ conducted a study on the incidence of anemia in women of the low income class in Montreal; 1451 women in apparently good health were examined. Anemia was said to be present if the hemoglobin level was less than 80 per cent (12.5 Gm.) of hemoglobin; 43.2 per cent exhibited hemoglobin levels less than 80 per cent; 8.5 per cent showed hemoglobin levels less than 70 per cent whereas definite anemia (50 to 59 per cent) was present in only 2.8 per cent of the women studied. The anemia was almost always of the hypochromic type. The hemoglobin percentage curve fell gradually through the reproductive period (from puberty to the menopause) due to the normal physiological iron requirements for growth, menstruation, pregnancy and lactation Following the menopause, there was a sharp diminution in the number of cases showing anemia. Repeated pregnancies did not appear to have any definite effect upon the incidence of anemia in the subjects studied. Menstrual loss was. however, of great importance. The approximate protein diet of 50 cases with hemoglobin levels between 75 to 100 per cent was compared with 50 cases with levels between 25 to 65 per cent, less protein in the form of beef, pork, liver, chicken, and eggs was consumed by the anemic persons The low iron content of the diet of many women of the poorer classes is apparently insufficient to keep pace with the demands conditioned by pregnancies and menstruation.

F. H. Bethell, S. H. Gardiner, F. MacKinnon⁵⁶ studied the influence of iron and diet on the blood in pregnancy. The basic diet recommended for pregnancy as formulated by the League of Nations Technical Commission provides a daily protein intake of approximately 80 Gm. including meat and eggs and adequate quantities of vitamins A, B₁, riboflavin, nicotinic acid, C, and D. Normal hematological values in pregnancy are difficult to define because of the often marked changes in blood volume with resultant hydremia. A red cell count of less than 3 5 million and a hemoglobin value of less than 100 Gm. (about 67 per cent) were considered as evidence of true anemia being present (54 per cent of the cases showed true anemia). Most cases of anemia in pregnancy are iron deficient (hypochromic), but some are due to "dietary deficiency" and have somewhat elevated mean corpuscular volume and color indices. The trend of hematological values varies during pregnancy, the lowest values being present at about the 6th month, increases beginning during the ninth month. Cases of anemia receiving iron (FeSO₄) (15 grains—1 Gm daily) showed much higher hemoglobin and red cell values at the end of pregnancy than those not receiving this medication This justifies the routine administration of iron throughout pregnancy, although cases not showing demonstrable anemia did about the same with or without iron. In the "diet deficient" group with socalled macrocytic anemia, improvement of the diet, particularly with respect to the intake of animal protein, was followed by a significant increase in blood values

The chronic hypochromic anemia of adult women ("primary" or "idiopathic"

hypochromic anemia) is considered by W. M. Fowler and A. P. Barer.⁵⁷ Menstrual hemorrhage, pregnancies, inadequate iron intake in the presence of achlorhydria account for most of these cases. Most observers recommend ferrous salts, particularly the sulfate, in doses of 12 to 16 grains (0.78 to 1.03 Gm.) per day.

Aplastic Anemia

M. M Wintrobe, A. Stowell, and R. M. Roll⁵⁸ report a case of aplastic anemia following gold injections, in which recovery occurred. A review of the cases of aplastic anemia, granulocytopenia, and of thrombocytopneic purpura since Dameshek's review in 1933 is given. The dangers of gold therapy as well as the rarity of recovery if aplastic anemia develops are pointed out

Hemolytic Anemias

C J. Roos⁵⁹ studied the quantitative urobilinogen content of the blood plasma. At times, there is marked discrepancy between the blood and urinary urobilinogen content. The importance of determinations of the fecal urobilinogen content is pointed out by W. H. Barker 60 The average daily output of urobilinogen in the feces is regarded as an index of the rate at which erythrocytes are being destroyed in the body. Abnormally high values were obtained in the cases of hemolytic anemia and in most of the cases of pernicious anemia in relapse The anemia of leukemia is occasionally hemolytic; this is also rarely the case in aplastic anemia. Transfusion of wellmatched blood may at times be followed by a striking increase in the excretion of bile pigment, suggesting that the better part of the transfused blood was rapidly hemolyzed The liver function tests were often significantly altered in the cases studied, suggesting a possible

relationship of diminished hepatic function to certain cases of "refractory anemia" or even leukemia.

L. Heilmeyer⁶¹ discusses newer concepts regarding the pathogenesis of hemolytic icterus. Contrary to the generally accepted theory that the bone marrow is at fault in congenital hemolytic jaundice with the resultant production of small, thick, unusually fragile erythrocytes, Heilmeyer believes that spherocytosis can be produced by various abnormal conditions, particularly those residing in the spleen. Certain cases of acquired hemolytic icterus are present in which the spherocytosis and the increased fragility are entirely due to "hypersplen-1sm" The exact mechanism of the hemolytic process is not clear

The Reviewer and co-workers⁶² have made almost identical conclusions based on clinical and experimental work Cases of acute hemolytic anemia, acquired type. which showed spherocytosis and increased saline fragility, responded well to splenectomy with a resultant normal blood picture Certain of the cases showed a circulating hemolysin which was capable of hemolyzing red cells in vitro When the patients recovered, the hemolysin disappeared indicating a possible causal relationship. Hemolytic anemia was then produced experimentally in guinea pigs with a hemolytic serum (hemolysin) comparable to that found in the human cases It was possible to produce varying degree of spherocytosis and increased fragility of the red cells by this means, indicating a direct action upon the red cells and not a defective marrow. It was concluded from these and other observations that hemolysins of various types were probably at the basis of all the hemolytic processes and that increased fragility was simply an expression of increased hemolytic activity within the body.

U. Ebbecke⁶³ discusses spherocytosis and its relationship to hemolysis and the sedimentation rate. The normocyte, under the influence of various hemolytic factors, becomes first the poikolocyte, then the small round thick cell called the spherocyte. Spherocytosis is the forerunner of hemolysis. This is also the conclusion reached by W. Dameshek, S. O. Schwartz and Karl Singer.64 Spherocytic red cells, because of their diminished ability to form good rouleaux, show a greatly diminished sedimentation rate. M. Vaughan⁶⁵ studied the characteristics of the red blood cells in acholuric jaundice (congenital type). Increased saline fragility was found in all cases and was almost invariably associated with spherocytosis Following splenectomy, increased fragility persisted but spherocytosis was lost in 50 per cent of patients.

The persistence of increased fragility suggests a fault in erythropoiesis, but the loss of spherocytosis indicates that the spleen has something to do with altering the red cell shape. Vaughan suggests therefore that both erythropoiesis and splenic function are at fault in familial hemolytic jaundice; the fundamental abnormality is not the spheroevtosis, as many have maintained, but some other factor. The Reviewer has maintained that the fundamental disturbance lies in an abnormal production of hemolysins with resultant spherocytosis and increased fragility. Following splenectomy, hemolytic production may continue, though at a greatly diminished The cause of the continued abnormality in saline fragility continues, as Vaughan states, to be obscure According to Bergenhem and Fahreus, the spleen acts upon the blood plasma producing a "lysolecithin" which is responsible for normal blood destruction. Karl Singer⁶⁶ has developed a micromethod

for testing the lysolecithin content of serum; it is not increased in hemolytic anemia. Singer has also shown that the red cells of congenital hemolytic jaundice are abnormally fragile to lysolecithin; whereas spherocytes in other conditions (acquired hemolytic icterus) react like normal red cells to this lysin. The concept of "differential fragility" has been discussed by W. Dameshek, S. O. Schwartz, and Karl Singer.⁶⁴ The lysolecithin content of the splenic vein blood may perhaps be correlated with the fact that the titer of complement in this vessel is 10 to 50 per cent higher than in the peripheral serum, 67 Several articles have been written on "macrocytic hemolytic anemia" Most of the cases reported are those in which spherocytosis is not marked and an apparent macrocytosis due to a well-marked reticulocytosis is present. Some of the cases are associated with hepatic disease in which macrocytic anemia is commonly present. The Reviewer⁶⁸ has criticized the designation of "macrocytic" for many of these cases which are in reality examples of acquired hemolytic icterus of the acute or subacute varieties. The concept that an acquired form of hemolytic icterus is present seems to have been almost wholly discarded, despite the appearance of many recent cases "Lederer's anemia" or "macrocytic hemolytic anemia" are usually diagnosed.

C. S. Dyke and F Young⁶⁹ report cases of macrocytic hemolytic anemia associated with increased red cell fragility. In these cases, the mean cell diameter was determined by the halo method and many spherocytes may well have been present. Price-Jones curves were not done. C. J. Watson⁷⁰ also reports on the macrocytic or acquired type. That microcytosis is pathognomonic of the congenital type has been disproved by the Reviewer, who has dem-

onstrated it in various acquired and symptomatic cases of hemolytic icterus. Watson's macrocytic cases were associated with cirrhosis of the liver, Hodgkin's disease, and leukemia in all of which macrocytosis is certainly not infrequent. They were not apparently of the "idiopathic" type of acute cases of acquired hemolytic icterus described by the REVIEWER. Watson's paper brings out various interesting points, however: the presence of autohemagglutination, the effect of epinephrine on increasing the red cell count just prior to splenectomy, the coexistence of severe hepatic disease with hemolytic jaundice, and the importance of studying the fecal urobilinogen.

Acute hemolytic anemia following the administration of sulfanilamide is occasionally reported Two fatal cases are reported by H Wood⁷¹ and Simon Koletsky 72 Two nonfatal cases in which the serum showed autoagglutination of the red cells were studied by William Antopol, Irving Applebaum, and Lester Goldman 73 The presence of autoagglutination in acquired hemolytic jaundice was stressed by Widal and his co-workers 30 years ago, but has since then been mostly forgotten. Antopol and collaborators point out that this abnormality may serve as a source of error in blood grouping tests

One of the most dramatic events in medical practice is the effect of splenectomy in a patient seriously ill with the hemolytic crisis of congenital hemolytic icterus or with acute (acquired) hemolytic anemia. Within a few hours after operation, there is usually a remarkable improvement both in the appearance of the patient and in his sense of well-being. Splenectomy should be considered in every case of these 2 different, but similar physiological conditions. The patient should first be prepared by 1 to

3 transfusions of carefully matched citrated blood of the same blood group given slowly (Bank blood should not be used). If evidences of hemolysis continue and it is seen that the patient has not recovered from transfusions alone, splenectomy should be performed without further delay. Too many transfusions may result in severe reactions and overburdening of the circulation; too much delay may result in a dead patient. These cases require careful and intelligent handling and represent as much of an emergency situation as diabetic coma.

Of 12 cases recently observed by the Reviewer, 7 made dramatic and sustained recoveries; 3 died shortly after operation; and 2 relapsed. Of these, 1 has died and the other is in serious condition. W. DeW. Andrus and C W. Holman⁷⁴ report the results of splenectomy in 50 cases of various blood disorders. In many cases with large spleens. particularly in hemolytic acterus, the injection of 15 minims (1 cc.) adrenalin just before delivering the organ was of great aid in bringing about considerable contraction, thereby facilitating its delivery into the wound and also expressing some splenic blood in the general circulation Seventeen splenectomies in hemolytic jaundice were performed without operative death However, 12 of the cases had hemoglobin levels of 50 per cent or over, which is quite different than in the above series of the REVIEWER, in which the preoperative level of hemoglobin was always between 20 to 40 per cent W. P. Thompson⁷⁵ discusses typical and atypical hemolytic anemias with the end results of splenectomy The results were uniformly good (except in one case) in the typical familial group, but very poor in the atypical group, most of the latter patients having died.

Atypical Hemolytic Anemias

Sickle Cell Anemia—L. W. Diggs and J. Bibb⁷⁶ describe very carefully the red cell characteristics in sickle cell anemia. The percentage of typically sickled cells is not related to the severity of the anemia. "Mexican hat" cells (Haden) or "Target cells" (Barrett) are common; these cells are shaped like a bull's eye or target in stained preparations and according to A. M. Barrett⁷⁷ are more resistant than normal red cells to hypotonic solutions of salt. fragility test in sickle cell anemia is almost invariably abnormal with an increased resistance span. The resistance to mechanical trauma in a shaking apparatus was, however, diminished. The sedimentation rate was much slower than in cases with normal blood cells due to the fact that in the presence of sickling, the aggregation of rouleaux is greatly hindered. J. M Arena⁷⁸ reports 5 cases in children notable because of the appearance of cerebral vascular disturbances. occasionally fatal Capillary stasis due to distortion and agglutination of red cells and other factors such as fever and infections probably contribute, Arena believes, to the tendency to capillary engorgement and arterial thromboses

Erythroblastic Anemia — D W Atkinson⁷⁹ points out the various clinical features of Cooley's anemia which is usually present in young children and is ordinarily fatal before puberty. The two cases described have been followed for 13 years and are now aged 17 and 20. The girl of 20 began to menstruate at the age of 16 and is asymptomatic, no nucleated red cells were recently seen. This is apparently a very mild case which may be more or less "burnt out". The brother, aged 17, has had a much more stormy course, perhaps because splenectomy was done at the age of 6. Showers

of nucleated red cells have persisted without much change over the years. The treatment has consisted of iron in large doses. The author quotes Cominopretros, who found that certain relatives of individuals with the disease showed an increased resistance of the red cells to hypotonic solutions of salt; these individuals might be the carriers of the disease. The red cells of Cooley's anemia, in contradistinction to those of congenital hemolytic jaundice, show a decreased fragility.

Polycythemia

S. B. Nadler and I. Cohn80 report 4 cases of polycythemia in 1 family These cases were associated with a high circulating blood volume but, unlike most cases of polycythemia, there was no increase in leukocytes, polymorphonuclear cells, or basal metabolic rate. It is concluded that "familial" polycythemia should be included amongst the cases of true polycythemia. H. R. Miller⁸¹ reports on the high incidence of coronary artery thrombosis in polycythemia vera as based on 7 cases which came to post mortem examination, of these 3 showed the evidences of coronary artery occlusion. N Rosenthal and F. A. Bassen⁸² present an interesting study on the course of polycythemia based on an analysis of 13 cases The disease may be asymptomatic and discovered accidentally may be of many years' duration. Extremely high platelet counts were present in about 30 per cent of 75 cases, in these thromboses were common Much stress is laid upon the evidences of leukoblastic activity and upon the possibility that leukemia will eventually develop in many cases

"Spent" polycythemia may be associated with a chlorotic (low hemoglobin) tendency, with high platelet or leukocyte counts, or with osteosclerosis

Possibly belonging to the latter group of cases are the cases of "leukoerythroblastic anemia and myelosclerosis" as reported by J. M. Vaughan and C. V. Harrison.83 These cases both showed initial polycythemia but when studied several years later showed splenomegaly, irregular density of the spongiosa of the bones, anemia with leukocytosis and thrombocytosis, increased saline fragility, and fibrosis of the marrow. R. L Haden⁸⁴ discusses the red cell mass in polycythemia with relation to diagnosis and treatment. The red cell mass is determined from knowledge of the volume per cent of packed red cells (hematocrit) and the total blood volume. The red cell count per cmm does not accurately measure the total increase in the mass of red cells within the body since the red cells are apt to be small and hypochromic, whereas the red cell mass per kilogram is the most sensitive indicator

Treatment—Haden believes that the treatment of polycythemia should based on the total red cell mass Reviewer has come to somewhat similar conclusions except that in practice, use of the hematocrit reading for an indication of the total red cell mass is justi-Therapy should be directed to lowering the hematocrit and maintaining it at a normal level (approximately 46 per cent). After the establishment of an iron deficiency state by repeated frequent (usually 2 per week) venesections of 1 pint (500 cc) each, continuation of the iron deficiency state is maintained by a diet low in 110n. The red cell count may rise in 3 to 4 months, but as long as the hematocrit remains at essentially normal values, no further treatment is necessary. Ordinarily, cases will go along for 8 to 15 months between series of venesections.

A diet low in iron or protein alone has not been found effective in our cases,

although F. Herzog and G. Kleiner⁸⁵ report striking results in 19 cases with a diet extremely low in animal protein. F. Andersen, T. Geill and E. Samuelsen⁸⁶ treated a case of polycythemia with x-rays over the Brunner gland region of the stomach and duodenum with an excellent result. The idea was to diminish secretion in the area in which "intrinsic factor" is formed The authors believe that this method is more rational than that of treating the bone marrow with x-rays. The Reviewer's experiences with x-ray therapy in this disease have been disappointing; not only that. it seems unwise to expose an essentially normal individual with normal tissues to the powerful x-rays which may at some future time result in neoplastic proliferation.

Congestive Splenomegaly, Spleen-liver Syndrome Banti's Syndrome

M Rousselot⁸⁷ reports on the symptoms, signs, and results of treatment in these cases which, whatever their causes might be, are always associated with portal hypertension. The pressures in the splenic vein were invariably higher than in the peripheral veins. An excellent summary of the end-results of operation is presented. Splenectomy is contraindicated in cases of progressive decompensated liver disease portal hypertension in which there was splenic vein thrombosis or in which the obstructive factor could not be elicited the results were "gratifying" Hematemesis as a postoperative symptom is usually a grave prognostic omen C H Drenckhahn⁸⁸ advocates the prevention of esophageal hemorrhages by lowering the blood viscosity. This is accomplished by performing a venesection or two when it is thought a hematemesis will occur The decision for the correct time is based upon careful observation of the patient; in the 2 cases cited, hematemesis always occurred when the blood level reached a certain point. Venesections were therefore given when this point was reached with the result that hematemeses were avoided.

BLOOD TRANSFUSIONS

A. S. Wiener⁸⁹ gives a comprehensive review of the technic of blood grouping tests preliminary to blood transfusions. Certain important points are stressed, such as the advisability of using typing sera of high titer, the use of the test tube method, and the differentiation of subgroups of A & L. Davidsohn⁹⁰ discusses the possibility that severe transfusion reactions are at times due to the development of subgroups. This is particularly true when recipients belonging to Group A-II are given several transfusions. Davidsohn presents a rather complicated method for the recognition of the subgroups of A.

The subject of stored blood has received a great deal of attention, particularly in the British literature. Every part of London now has its blood bank and its quota of donors readily available for the expected emergency. The fighting forces are prepared to use large quantities of blood which are specially stored at the front for instant use. One wonders whether the Russians have as yet had the opportunity of utilizing their technic of extracting blood from cadavers for use in those still alive.

J. Scudder, C. R. Drew, D. R. Corcoran, and D. C. Bull⁹¹ report the first of a series of studies in blood preservation. This deals mainly with the daily increase in plasma potassium which develops as blood is stored. Potassium diffuses out of the cells into the

plasma, the least diffusion taking place in a 0.3 per cent solution of sodium citrate. Shaking hastens the loss of potassium from the cells; tubular containers are preferable to wide flasks. In certain states associated with high blood potassium values (dehydration, intestinal obstruction, severe burns) and perhaps in other conditions, as in renal and hepatic insufficiency, the rapid administration of large quantities of blood preserved too long may be dangerous.

J. A. Kolmer⁹² points out the various degenerative changes which take place in stored blood, swelling and increased fragility of the red cells; disintegration of the neutrophils, deterioration of the platelets, and loss of bactericidal and opsonic activity. Kolmer believes that citrated blood preserved at 39 to 43° F. (4 to 6° C.) may be useful in the treatment of acute hemorrhage and in shock for the restoration of volume, but is inadvisable for the treatment of anemia, blood dyscrasias and infections. Most reports are far more encouraging regarding the value of stored blood. Certainly it is a great comfort to have on hand in a large hospital a supply of blood which is available for instant use in an emergency The REVIEWER has not hesitated to use this type of blood for the therapy of anemia, when it is only red cells which are required (hypochromic anemia, aplastic anemia, anemia of leukemia, etc.). In hemolytic anemias, in agranulocytosis, and in thromboextopenic purpura fresh blood should by all means be used.

F E. Barton and T. M Hearne⁹³ describe the use of placental blood for transfusion. They recommend the method because it is "safe, economical, and efficacious". S. W. Sappington⁹⁴ recommends heparinizing the donor and then injecting the recipient with the donor's blood. This method is already

in use in several hospitals in Sweden and France. The donor is injected with pure heparin in the dosage of 1 mg. per kg of body weight; usually 1.5 cc. of a 5 per cent solution is required. Seven minutes later, the blood is withdrawn. Without further handling or assistance, the blood may then be injected into the recipient. Reactions have not appeared in Sappington's series. C. C. Sturgis and S. M. Goldhamer⁹⁵ present the indications for the use of transfusions in clinical practice.

HEMORRHAGIC STATES

Blood Clotting

W. H. Seegers and his co-workers⁹⁶ at the State University of Iowa describe further work in the purification of thrombin. The addition of calcium and thromboplastin to a prothrombin solution resulted in a crude thrombin which could be further purified. One cubic centimeter of a 1 per cent solution of this purified thrombin was effective in clotting 1 cc. of blood in 2 seconds By the use of a thrombin solution spray, these workers were able to stop the oozing from incised liver, bone, and brain tissue. Its application to clinical hemorrhagic conditions has thus far been slight, but the further results of the Iowa investigators are well worth watching.

The clotting of blood is taken up from another direction by J. H. Ferguson and B. N. Erickson,⁹⁷ who have studied the action of trypsin. This enzyme can clot citrated plasma without added calcium or cephalin. Trypsin may be one of a series of "thromboplastic enzymes" which causes the mobilization of calcium and thromboplastin about prothrombin with resultant formation of thrombin. Ferguson has furthermore been able to

activate the prothrombin of hemophilic "globulin substance" to normal thrombin with resultant clotting by the addition of pure crystalline thrombin. The plasma of hemophilics may be deficient in thromboplastic enzyme.

Hemophilia

In last year's review the studies by Pohle and Taylor on the coagulation defect in hemophilia were presented. At this time their experiments revealed a deficiency in the globulin fraction of the plasma. "Globulin substance" prepared from normal human plasma was found to hasten the clotting time for hemophilic blood in vitro and in vivo After several injections of "globulin substance," however, a refractory phase occurred so that the clotting time rose to its original level despite continued injections (F J. Pohle and F. H L Taylor⁹⁸) When normal or lyophilized plasma was injected, the refractory period was ended, indicating that whole plasma contained a substance that was effective.

In a more recent publication E. L. Lozner, R. Kark, and F. H. L. Taylor⁹⁹ state that normal serum from which prothrombin and fibrinogen had been removed was still capable, when injected, of causing a prompt fall in the coagulation time of blood of hemophilia in vitro and in vivo. It was suggested that the loss of effectiveness of the globulin substance might be in the presence of a factor in normal plasma which was lost in the acid precipitation of the globulin substance. Therefore, globulin was prepared by dialysis by E. L. Lozner and F. H L. Taylor¹⁰⁰ and such a preparation of euglobulin was found to resemble normal human plasma in its ability to maintain in hemophilia a reduced level of the blood coagulation time when injected intravenously every 6 hours

Vitamin K

During the last few years, outstanding advances have been made in the troublesome and dangerous hemorrhage of iaundice. In obstructive jaundice or biliary fistula where bile salts do not reach the intestinal tract, poor absorption of fat-soluble vitamins results. In the absence of fat-soluble vitamin K there may be a lowering of the plasma prothrombin, one of the factors in normal clotting, with a resultant tendency to bleeding. The plasma prothrombin level can be sustained by giving vitamin K concentrates and bile salts per os. Blood transfusion is a rather inefficient method of combating the bleeding tendency due to hypoprothrombinemia, as its effect is slight and transient. In one patient there was a measurable increase of only 6 per cent of plasma prothrombin after a 20-ounce (600 cc.) transfusion.¹⁰¹

Rapid progress has been made in the chemistry of vitamin K. A rather large number of compounds with vitamin K activity have been found, and several of these have been identified and synthesized. The first is phthiacol. All of these compounds have a 10 carbon ring of naphthalene with an atom of oxygen in the 1 and 4 positions forming the basic substance naphthaquinone. When oral administration is uncertain because of vomiting, phthiacol in a 0.2 per cent solution may be given intravenously. 102

The mechanism by which prothrombin is formed and its dependence on vitamin K are not understood. The liver has been regarded as the site of prothrombin formation because hepatotoxins such as chloroform cause a plasma prothrombin deficiency and because some patients believed to have severe liver damage have failed to respond to large amounts of vitamin K and bile salts. In the dog, total hepatectomy causes a rapid fall in plasma prothrombin. 103

Until recently, the mechanism of hemorrhage in the condition known as hemorrhagic disease of the new born has not been understood. In a study of 20 new born infants, W. W. Waddell, Jr. and DuP. Guerry, III¹⁰⁴ have shown that their prothrombin and blood clotting times are unusually high, especially between the second and sixth days of life, which corresponds to the time at which hemorrhagic disease almost always manifests itself. Administration of vitamin K concentrates orally kept the prothrombin and blood clotting times normal. Routine use of such therapy in the infant or possibly in the mother late in pregnancy may be the answer to the prophylaxis of many cases of intracranial hemorrhage during birth, and occasionally fatal bleeding following surgical procedures such as circumcision early in life. C. A. Owen, G. R. Hoffman, S. E. Ziffren and H. P. Smith¹⁰⁵ made similar observations and in addition noted a discrepancy in the values obtained by the "2-stage" and the Ouick methods.

D. Warner, K M. Brinkhous, H. P. Smith, S. E Ziffren and their coworkers¹⁰⁶ who have contributed so much to our knowledge of vitamin K have also simplified the prothrombin clotting test so that an easy bedside method is now available which correlates well with the more complicated procedures Thromboplastin is prepared by grinding fresh lung of ox or rabbit To each 10 Gm 10 cc of 09 per cent saline is added and stirred at intervals for a few hours. The mixture is then strained through gauze and kept in the ice box when not in use One-tenth cubic centimeter of the resultant filtrate (or thromboplastin) is added to each of 2 serologic tubes. Freshly drawn blood from the patient and a normal is added to the 1 cc mark of each tube and the latter tilted every second until

clotting occurs. The clotting activity of the patient expressed in per cent is determined by the ratio of the clotting times in seconds of the normal to the patient and multiplied by 100.

Thrombocytopenic Purpura

Very little that is new has been written of thrombocytopenic purpura in the past year. Some new cases of sedormid purpura are reported. T. McGovern and I. S. Wright¹⁰⁷ point out that sedormid may cause a serious hemorrhagic syndrome. They advise restriction of its sale except on a physician's prescription and caution on the part of the physician in recommending its use small sensation was occasioned by the appearance in 1938 of data purporting to show that spleen extracts from cases of thrombocytopenic purpura resulted in marked reduction in platelets in rab-The substance causing this reduction was named "thrombocytopen" 108 Numerous investigations in the attempt to confirm this phenomenon have, however, proved uniformly unsuccessful

LEUKEMIA

This interesting question of the relationship of trauma to leukemia is discussed by A. Yaguda and N. Rosenthal 109 Although the cause of leukemia is unknown, certain factors such as infection, hemorrhage, and trauma may play a part in the development of symptoms in a latent case. Because cases in which a history of trauma is present may result in legal action, they are of definite importance Lowson in 1930 collected 40 cases from the literature in which trauma was followed by leukemia. Yaguda and Rosenthal state that cases which develop leukemia shortly after trauma must be considered as bearing a definite relationship between the trauma and the leukemic manifestations. The injury results in an aggravation of a pre-existing or asymptomatic leukemic state rather than as a direct etiological factor.

J. Furth and O B. Furth, 110 report the development of monocytic leukemia in mice following the intrasplenic injection of an anthracene compound: 1-2 benzpyrene. These observations further evidence of the neoplastic nature of leukemia. F. R. Miller and Heinle have produced in guinea pigs a leukemiclike picture both in the blood and tissues by the injection of urine extracts from patients with various types of leukemia. This work is very interesting and suggestive of an infectious or metabolic etiology, however, confirmation is desirable before it can be accepted.

The clinical and pathological aspects of acute leukenna are discussed by C. E. Forkner ¹¹¹ Forkner maintains that marked swelling of the mucous membranes, particularly of the gingivae, is characteristic of acute monocytic leukenna. The Reviewer can only partially agree with this statement, since cases of typical acute lymphatic leukenna not infrequently present as marked mucous membrane changes as those with the monocytic variety

It is sometimes easier to differentiate the cell type from the clinical features than it is from the hematological. Generalized lymphadenopathy is usually lymphoid; marked gingival and skin changes go with the monocytic, moderate splenomegaly without adenopathy with the myeloid form. However, in cases in which differentiation is difficult, the supravital and peroxidase technics may be of value. Infectious mononucleosis, acute disseminated miliary tuberculosis, whooping cough with marked lymphocytosis, agranulocytosis, and occasionally neo-

plasms may give leukemoid blood pictures.

A. R. Rich, M. M. Wintrobe and M. R. Lewis¹¹² present a very interesting and important motion picture study of the cells of normal bone marrow and lymph nodes and of leukemic blood. Motion pictures of leukemic cells in hanging-drop tissue culture preparations reveal that the myeloblast can be readily distinguished from the lymphoblast by its "writhing, corkscrew or wormlike" motility, the lymphoblast having the appearance of a "hand mirror" The latter cell in these preparations moves forward in 1 direction in a "steady, unperturbed manner." The monocyte or histocyte exhibits very active motility of a pseudopodic type, often in several directions at once Ordinary mature lymphocytes, which by most observers have been regarded as without motility in fresh wet preparations, exhibit striking motility in these hanging-drop tissue cultures These observations provide a new type of evidence against the "unitarian" interpretation of blood formation which assumes, on the basis of the appearance of the cells in stained preparations, that lymphoblasts and myeloblasts are identical

M Booth and R R Rembolt¹¹³ present a review of leukemia in childhood A number of valuable data relating to classification, diagnosis, and treatment is given B S Leavell¹¹⁴ studied the incidence and factors influencing the duration of life in chronic leukemia. The average duration of life after onset of symptoms in the lymphoid type was 3.2 years, in the myeloid type 3.6 years. Four per cent survived 10 years or more. The duration of life was shorter in patients with marked anemia.

H E Freeman and Simon Koletsky¹¹⁵ discuss the cutaneous lesions of monocytic leukemia, both of the acute

and chronic (reticulosis) variety. This type of leukemia may exhibit nonspecific lesions of the skin similar to those seen in the other varieties of leukemia: Purpura; urticaria, pigmentation, exfoliative dermatitis. The specific lesions consist of macules, papules, nodules, and plaques Mycosis fungoides may be simulated. The individual lesions change both in size and color; generalized dissemination is usual; the dermatologic features may be so outstanding as to dominate the picture and be treated some time before the underlying hematologic abnormality is recognized. X-ray treatment may result in a striking but only temporary effect.

A case of eosinophilic leukemia is reported by S. Thomsen and P. Plum ¹¹⁶ In this case there was striking eosinophilia for most of the course of the disease with the terminal blood picture showing large numbers of myeloblasts. The true cases of eosinophilic leukemia are rare; most cases in which the diagnosis is considered are examples of infection, allergy, or Hodgkin's disease

Treatment—The treatment of acute leukemia is very unsatisfactory. X-ray therapy should not ordinarily be used unless there is something specific to reliefe as very thick gums, a very large spleen, or an extremely itchy skin rash Transfusions, liver extract, iron, large doses of the vitamins, yellow bonemarrow extract, etc., may be given with the understanding that they are being used mainly as "therapeutic gestures" They are perhaps justifiable from the possibility that an occasional remission may occur, whether or not this is related to the treatment, it is difficult to say In chronic leukemia, excellent results may be obtained, at times lasting for many months Best results in the Re-VIEWER'S hands have occurred with localized x-ray therapy over the spleen

in myelogenous leukemia and over the various sites of generalized lymphadenopathy in the lymphatic variety. During the course of therapy, transfusions may well be given.

LEUKOCYTIC NEOPLASMS

Hodgkin's Disease

P. Uhlenhuth and K. Wurm¹¹⁷ review the various concepts regarding the pathogenesis of Hodgkin's disease. Various infections, etiological agents, including a possible virus, are discussed. The Gordon test, in which some of the macerated gland tissue is injected into the brain of a rabbit, which is observed for ataxia, etc., is discussed. This test has been shown by Wurm and by Jackson, Turner, and Parker to be dependent upon the presence of eosinophils in the Hodgkin's process.

E. B. Krumbhaar (A Symposium in the Blood and Blood-forming Organs, Madison, 1939) reviews the present status of Hodgkin's disease. He reports preliminary data on tissue cultures from a typical case These studies (made by Mrs. Margaret Lewis) thus far indicate that the agent behind the proliferating cells is most likely infectious rather than neoplastic X-ray therapy may lengthen life considerably or even in a few cases restore the patient to indefinitely prolonged good health H Jackson, Jr 118 states that Hodgkin's disease may be subdivided into 3 types: Lymphoma, granuloma, and sarcoma. In lymphoma, mature lymphocytes predominate, among which are scattered typical Reed-Sternberg cells. In granuloma, there are fibrosis, eosinophilia, necrosis, and giant cells. In sarcoma there is invasion with large cells with prominent nucleoli. There are no distinctive blood pictures The basal metabolic rate is elevated with

widespread disease. In the average case the patient lives for $2\frac{1}{2}$ years after onset of symptoms.

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KIDNEY, DISEASES OF

By Francis D. Murphy, M D.

ACUTE NEPHRITIS

Bachr¹ believes that acute glomerulonephritis is a sharply circumscribed entity with a specific etiology and pathogenesis. It is part of a disease of the body as a whole and its chnical manifestations are related to pathologic phenomena in various parts of the body. He disagrees with the conception of Bell that acute nephritis is an advanced stage of certain changes which are often found at death in various diseases A positive diagnosis of acute glomerulonephritis, according to Baehr, can be made only if there are clinical evidences of vascular disturbances, such as hypertension and edema, in addition to urinary changes. This idea is at variance with many writers who contend that the diagnosis of acute glomerulonephritis should be made

in the presence of urinary anomalies alone He believes that "the sudden explosive occurrence of acute glomerulonephritis is a specific reaction concerned in some unknown manner with the mechanism of recovery from streptococcal infections"

Etiology and Pathogenesis — The fact that in patients with rheumatic fever or Bright's disease there is an increased allergic irritability to rabbit serum and that the allergic irritability is further increased in those individuals who have had recent focal infections has been shown by Schultz² In the cutaneous tests, hemolytic streptococcus, nucleoprotein and tuberculin were used along with the rabbit serum Correlation between the 3 test substances and an increased allergic irritability could only be established to the extent that secondary reactions to rabbit serum were not observed among those patients who had not recently experienced a focal infection and in whom hypersensitivity to both nucleoprotein and tuberculin were negative. This is further evidence that alterations in tissue reactivity are associated with both the rheumatic and nephritic states.

The following observations made by Arnott and Matthew³ are based on the fact that in hypertensive cases the blood flow is normal, the narrowing of the arterioles causing an increased resistance which is balanced by the rise in blood The removal of the factor pressure causing narrowing of the arterioles, vasoconstrictor influence, will increase the blood flow since the head of pressure or hypertension remains constant. They estimated the blood flow in the hand after inhibiting the nervous constrictor tonus, using the heat elimination of the hand as an index of blood flow Pickering had previously shown that, whereas the blood flow in chronic hypertension fell within normal limits, in acute hypertension it was greater during the hypertensive phase than during the subsequent normal phase Arnott and Matthew found that in acute glomerulonephritis the maxmum heat elimination was considerably higher during the hypertensive phase than during the subsequent period of normal blood pressure. These results suggest that in transitory hypertension of acute glomerulonephritis there is an abnormally high degree of vasoconstrictor tonus

Feller and Hurevitz⁴ studied 2 cases of acute nephritis with cardiac failure In 1 case a biopsy of the deltoid muscle revealed a subacute perivascular inflammation involving particularly the arterioles. As the patient recovered, a second biopsy showed that the perivascular process was less severe and of a

more chronic nature. In another case of acute nephritis, a biopsy taken from the pectoralis major at the time of autopsy revealed an inflammatory lesion of the arterioles. This lesion was also found to be widespread and included the arterioles of the heart, but the glomerular damage was minimal. This has led the authors to conclude (a) that acute nephritis is part of a widespread vascular disease which is occasionally severe enough to be called panarteriolitis and (b) that many patients who seem to have acute nephritis with cardiac failure actually have panarteriolitis with involvement of the vessels of the myocardium.

In their study of 55 patients with acute hemorrhagic nephritis, Rubin and Rapoport⁵ cite the work of Longcope and his co-workers which showed that the hemolytic streptococcus is associated with acute hemorrhagic nephritis. Since myocardial damage is a fairly frequent complication of acute hemolytic streptococcic infection, it is possible that the same infection responsible for the acute nephritis also damages the heart. The second factor, hypertension, they believe, is immediately responsible for the impairment of cardiac function. Hypertension was present in all patients with acute hemorrhagic nephritis showing signs of cardiac insufficiency. In evaluating the reading of children's blood pressure it was noted that the blood pressures which were not called abnormal at first were elevated in comparison to values obtained after the patient recovered was found that the elevation of the diastolic pressure is a more characteristic finding than elevation of systolic blood pressure. In the 14 patients reviewed, those who had the cardiac damage did not show a more severe nephritis than those with no cardiac involvement. The only deaths which occurred in the series

of 55 nephritic patients were due to cardiac failure.

The occurrence and significance of myocardial failure in acute hemorrhagic nephritis were also studied by Whitehill, Longcope and Williams.6 The symptom which indicated the possibility of some circulatory failure was dyspnea, particularly when it was paroxysmal or nocturnal or was combined with orthopnea in the absence of pleural effusion and ascites. The signs were enlargement of the heart, accompanied by alterations of the impulses and sounds, elevation of venous pressure, and enlargement of the liver In their series of 138 cases, 98, or 71 per cent, showed clinical signs of cardiac insufficiency The actual cause of the failure of the heart is not known, but it is conceivable that the smaller vessels of the myocardium may be involved in the vascular lesion by vasoconstriction as suggested by Langdorf and Pick This might bring about an extensive temporary damage to the muscle and the accompanying circulatory failure might lead to an increase of subcutaneous, cerebral or pulmonary edema, thus interfering with the functions of the injured kidney. The invocardial tailure varies in its severity in direct proportion to the severity of the nephritis. The authors believe that the use of digitalis in full doses has benefited some of the patients with severe circulatory failure

Studies of the bone marrow in various types of nephritis were made by Nolli.7 In renal sclerosis with anemia from old age there is hypoplasia. In acute glomerulitis with anemia the changes are of the type seen in acute and subacute forms of posthemorrhagic anemia. In diffuse chronic renal inflammation, the hematopoietic functions are diminished. The myelopathy causes morphologic changes of the erythrocytes and diminution of their number in the peripheral blood.

Treatment with a combination of arsenicals, iron and liver extract early in the development of the renal disease controls the functional disorders of the bone marrow.

A series of 150 cases of acute nephritis was discussed by Murphy and Rastetter8 with special reference to the course and prognosis. They point out that more attention should be paid to the early recognition of acute nephritis and that one should not demand the full classical textbook picture before making a diagnosis. In their opinion, if milder forms of nephritis are recognized and treated, some patients will be saved from developing chronic nephritis The fundamental principle in treatment is complete rest in bed until all evidence of kidney inflammation has disappeared Removal of foci of infection and attention to certain dietary details are also emphasized.

In a follow-up study of cases of acute nephritis previously reported, Tallerman and Burkinshaw⁹ find that after 8 years the number of cases that can be classified as completely recovered has decreased

Treatment——In the treatment of acute nephritis, it is a generally accepted fact that *bed rest* should be maintained until the active inflammation has subsided or the transition to chronic nephritis has been established. Healing is indicated by normal renal function, absence of hematuria and a normal sedimentation rate. In addition, during the acute initial phase the complications which lead to a fatal termination must be guarded against

In a discussion of the treatment of acute nephritis, Rubin and Rapoport⁵ state that if the heart seems normal, if there is no elevation of the blood pressure and if the major disorder is the disturbance of toxic metabolites, therapy might include **forcing of fluids**. When

acidosis appears, they recommend the administration of alkali, such as sodium lactate. In 1 of their cases in which anuria was present, fluids were given in large amounts, and despite the increase of edema the intoxication was lessened. After 5 days the anuria disappeared and diuresis was established. If hypertension is present in the course of acute nephritis, its control is important. Fluids should be restricted as a further adjunct in the treatment of hypertension with myocardial damage. They also recommend the intramuscular injection of 50 per cent magnesium sulfate in a dosage of 1.4 minims per pound (02 cc. per kilogram) of body weight. Since the studies of Pickering showed convincing evidence that the hypertension in acute nephritis is due to vasospasm, experimental work has been done which shows that magnesium relieves hypertension in rats produced by ergotamine tartrate which causes a vasospasm. It was observed that magnesium carbonate added to the diet of rats prevented hypertension if given before the administration of ergotamine tartrate, and when given to animals after hypertension had been produced the blood pressure returned to normal.

In a 7-year-old boy with acute hemorrhagic nephritis and hypertension additional observations were made concerning the action of magnesium in reducing hypertension The patient was put on a constant intake of fluid (1 oz -30 cc.) per hour and hourly determinations of the output of urine were made. Three ounces (90 cc) of a 50 per cent solution of sucrose were given intravenously This was followed by marked diuresis but no drop in blood pressure. Fourteen hours later a 50 per cent solution of magnesium sulfate was given intramuscularly (0.2 cc. per kilogram of body weight). Following this, there was a

prompt drop in both the systolic and diastolic blood pressures with no diuresis.

Rubin and Rapoport also found beneficial effects from intramuscular injection of magnesium sulfate in patients with hypertensive encephalopathy, and although these effects have been ascribed to dehydration, clinical experiments indicate that the improvement is due to the relief of vasospasm. The effect of a single dose of magnesium sulfate is usually prompt, and the systolic and diastolic pressures are lowered within an hour and tend to remain so for several hours. The first dose can be repeated at 4-hour intervals. One caution must be observed, and that is in cases with marked impairment of renal function and low urinary output and in which there is retention of metabolites an accumulation of magnesium might occur with a resultant narcotic effect. The authors did not encounter this ill effect. Additional measures which are recommended in the treatment of cardiac damage are digitalis, oxygen, sedation, and possibly phlebotomy if advanced cardiac failure is present.

De Filippi¹⁰ used **Volhard's treatment** in 7 cases of acute nephritis. This consists of suppression of food and water for 5 days and administration of $2\frac{1}{2}$ to $3\frac{1}{3}$ oz. (75 to 100 cc.) of orange juice during the first 2 days, increased to 20 oz. (600 cc.) during the last 3 days. The diet is then gradually established over a period of 2 weeks, the orange juice being continued. He obtained good results. The treatment was well tolerated and acute cardiac and renal complications and chronic renal disease did not follow

In acute nephritis, Murphy¹¹ believes a diet low in protein and acid content should be given to lessen renal irritation. The height of the acute stage is short and no attention need be paid to the ca-

loric requirement A diet of 40 oz. (1200 cc.) of fruit juices, mild and cooked fruits is adequate. Fluids should be kept at about 50 oz. (1500 cc.) a day unless hypertension and increased intracranial pressure becomes severe when it may be advisable to reduce the amount for a time. With threatening uremia associated with vomiting and a disturbed electrolyte balance, 50 oz. (1500 cc.) of normal saline intravenously will help restore the balance.

The effect of tonsillectomy on the incidence and recovery of nephritis was observed by Illingworth 12 He found that 20 per cent of the patients with acute nephritis had had a tonsillectomy while only 9 per cent of the children, according to the general incidence of tonsillectomy in London, might be expected to have had the operation. In 5 per cent of the cases of acute nephritis, tonsillectomy was considered to be the cause of the disease. No cases of acute nephritis seemed to be benefited immediately or subsequently by tonsillectomy He therefore concluded that tonsillectomy does not prevent nephritis but may predispose it; the operation neither cures acute nephritis nor prevents it from progressing to the chronic stage

An investigation of the effect of sulfamiliamide given in therapeutic doses for long periods to rats with nephrotoxic nephritis was made by Smadel and Swift 13 They found that the course of experimental disease was not affected Rats with nephrotoxic nephritis but without renal failure excreted sulfanilamide in the same amounts as did normal rats Retention of sulfanilamide, which may occur in patients with severe nephritis, was not noted However, none of the rats developed renal failure. Normal rats which did not receive nephrotoxic serum excreted normal urine throughout the experiment.

CHRONIC NEPHRITIS

Symptoms and Clinical Course—It is the belief of Bell¹⁴ that the symptoms and clinical course of glomerulonephritis are dependent upon the character and extent of the initial lesion. If in the acute attack there is widespread severe capillary obstruction, renal insufficiency soon develops Those cases that terminate in uremia within a few months are called acute, while those that survive from 4 to 5 months to a year are usually called subacute When the initial lesion is less intense and the capillaries remain more or less permeable, a chronic nephritis develops Forty cases of hydropic glomerulonephritis (lipoid nephrosis) are reported In 6 of these the glomerular structure was that of chronic proliferative glomerulonephritis and in 9 others there was a mixture of proliferative and membranous glomerular lesions with the latter in great predominance remaining 25 cases there were no proliferative lesions.

In 6 cases in young children there were no visible changes in the glomerular capillaries and in 3 other children there were only focal membranous lesions With 1 exception, diffuse thickening of the basement membranes was present in all persons over 12 years of age There were no clinical distinctions between the 2 cases in children with thick membranes and those with normal membranes In those with diffuse thickening of the basement membranes hypertension was present in 14 and absent in 8 cases. When a patient with pure lipoid nephrosis develops hypertension and uremia no new disease is superimposed — there is merely progressive thickening of the basement membranes Nephrosis is a form of glomerulonephritis in which the glomerular capillaries remain open and allow the blood proteins to escape into the urine.

In proliferative glomerulonephritis, the capillary lesions are nearly always of the obstructive type

Etiology-By tying the vena cava above the entrance of the renal veins, Addis and Lew¹⁵ produced a transient anuria in rats resulting in an acute uremia. Before and after the procedure, the rats were given diets designed to induce wide variations in protein consumption and catabolism. None of the animals died when they were given diets in which the protein was low or which led to a moderate consumption of the proterns of milk and cereals On diets containing 9 per cent dry yeast, whose main protein constituent was casein, variations in the amounts of casein consumed had no effect on the mortality rate. On diets in which large amounts of proteins derived from dried liver, kidney and beef were consumed, the mortality was 8, 9, and 16 per cent respectively. A watersoluble extract of meat caused a 52 per cent mortality, but the alcohol-soluble portion of this extract produced no mor-The alcohol-insoluble fraction tality thus killed more than half the animals Suspecting that the toxicity was due to an morganic salt rather than an organic substance, a solution of potassium acid phosphate and potassium chloride was given in the same dose and was found to have the same effect as the alcohol-insoluble fraction of the water extract of meat. It can be concluded that the potassium was responsible for the high mortality when meat extract or alcohol-insoluble fraction of meat was administered and that it is probable that potassium was also a factor in the relatively high death rate following the consumption of large amounts of beef.

Using a different procedure, Bergman and Drury¹⁶ arrived at the same conclusions reached by Addis and Lew. Nephrectomized rats were fed urine from

fasting rats, rats allowed to drink a 10 per cent sucrose solution ad lib and rats allowed to eat meat ad lib. The survival time was 49 hours, 52 hours and 12 hours respectively. The urine from meatfed rats was obviously much more toxic. By separating the various constituents of the urine, the main toxic agent was found to be an inorganic fraction, either sodium or potassium. Further investigation showed that potassium was the harmful element and it is concluded that this is responsible for part of the toxicity of meat.

Treatment—Barborka¹⁷ recommends a diet essentially normal in protein and fluids, light in carbohydrate and low in fat for uncomplicated chronic nephri-In acute nephritis there should be marked protein restriction (25 Gm. at first, later raised to 50 Gm), fluids for proper drainage (1000 cc increased to 1500 cc) unless edema develops, low salt intake, restricted calories, high carbohydrate content and low fat intake. In chronic nephritis with edema, the protein content should be liberal providing the renal function is sufficient to permit its utilization without nitrogen retention. Fluids and salt should be restricted and the carbohydrate content high with no excess of fats in the diet. In nephrosis the diet should be high in protein (80 to 150 Gm and increased to 200 to 250 Gm if tolerated), high in carbohydrate content and low in salt, fat and fluid. For urenua a diet low in protein and salt and high in carbohydrate with an adequate supply of water (which means an increase in the effort to cause diuresis) is advocated.

Chronic renal insufficiency in which the renal lesion is progressively destructive, while the phenolsulfonphthalein excretion or blood urea concentration is within normal limits and remains so for years, is discussed by Addis.¹⁸ It is

pointed out that renal hypertrophy occurs in dogs on the basis of work hypertrophy when a unilateral nephrectomy is performed or when a double quantity of protein is given. When a unilateral nephrectomy is done, if the diet consists of 30 per cent casein a rapid and considerable increase of renal tissue results. If a 10 per cent casein diet is given, the compensatory hypertrophy is less, but the rate of increase at first is no slower.

The first rapid increase in renal tissue seems to be dependent on stores of protein in the body since if the body stores of proetin are depleted before nephrectomy the rate of increase is slower from the beginning The conclusion is that the most rapid and the greatest restitution of renal tissue will be obtained if plenty of protein is given However, Farr and Smadel have shown that in rats with glomerular nephritis an increase in protein hastened the rate of destruction of the kidney and shortened life. These results appear to be contradictory, but by grading the amount of work the kidney must do by maintaining an optimal amount of protein and varying it, thus reducing the work of the kidney, a favorable plan of action is possible. Most of the urine consists of urea, sodium chloride and water. The concentration of the sodium chloride and water in the blood plasm is not much different from that in the urine so their excretion requires relatively little work by the kid-Urea, on the other hand, may be concentrated 100 times in the urine, the result of a great deal of work on the part of the kidney Therefore, if kidney work is to be lightened, the rate of excretion of urea must be reduced by diminishing the amount of food protein.

Thus, considering food products in the light of the end-products of metabolism, carbohydrates and fats, ending in carbon dioxide and water, have no appre-

ciable effect on kidney work. Broth and meat extracts produce concentrated urinary constituents that can only increase kidney work and cannot be used for compensatory hypertrophy. Meat, fish and fowl all contain a good deal of nutritionally useless work-creating substances. but the proteins derived from milk, eggs and vegetables contain no creatinine or uric acid-forming substances. individual patient, a definite number of grams of protein a day must be decided on after determining the intensity and extent of the renal lesion and the amount of protein lost in the urine daily Weight. build and metabolic rate must be considered Thus the work of the kidney can be lessened and the compensatory hypertrophy of the renal tissue can be maintained by applying a theory which can be put into practice in the doctor's office

In chronic nephritis without edema. Murphy¹¹ believes that protein must be kept up to an amount that will supply the requirements of the individual Salt should be not too rigidly limited Fluids must be kept at about 2 quarts (2000 cc.) a day Marked restriction of salt may lead to a hypochloremia which may prove fatal and the administration of 1000 cc. of normal saline may save the patient at this time. In nephrosis and the nephrotic syndrome of chronic nephritis it is recommended that the patient be given the amount of protein necessary for proper nutrition, an adequate amount of fluid (50 oz —1500 cc. a day) unless developing edema demands further restriction and an amount of salt limited to that contained in the food itself, a so-called salt poor diet.

Lyon¹⁹ points out the beneficial action of the *basic ash régime* in chronic nephritis. Since animal protein is a rich source of acid radicles, it is kept at a minimum Lyon's diet consists mainly of milk, vegetables and fruits which are

mostly basic in character. He found that the pH of the urine in the basic ash diet ranged about 6.6 while on the acid ash diet it was lower—about 5.8. He concluded that patients with chronic nephritis progressed much more satisfactorily on a diet that was limited in meat, bread, eggs, and rice.

In the treatment of acidosis in renal insufficiency, Deakin²⁰ advises the use of **sodium r-lactate** by mouth or the intravenous administration of a sixth molar sodium r-lactate solution. He cites several cases in which the patients were in impending coma and were clinically improved after the administration of sodium r-lactate.

Renal Function Tests

The urinary excretion of sodium ferrocyanide as a test of glomerular function approximately parallels the results obtained with the urea clearance test, the phenolsulfonphthalein test and the renal concentration according to Stieglitz.21 Hydrated salt of sodium ferrocyanide, 0.5 Gm. dissolved in 10 cc. of sterile distilled water, is injected intravenously. The solution must be clear before the injection is made. Specimens are collected at 30, 60, 120, and 180 minutes after injection and their ferrocvanide content determined Normally the average output is about 15 per cent of the injected dose for the first 30 minutes. 25 per cent at the end of an hour and 35 per cent and 45 per cent at the end of 2 and 3 hours respectively. In hypertensive arterial disease without other evidence of nephritis the glomerular function was found to be impaired depression occurs also in acute and chronic nephritis during the first hours and for practical purposes, therefore, analysis at 30 and 60 minutes is satisfactory. The results obtained in hypertensive arterial disease without other evidence of nephritis suggests that occult glomerular injury depreciates the capacity of the glomeruli to excrete certain solutes promptly.

Observations by Hayman, Martin and Miller²² showed that in chronic glomerulonephritis and nephrosclerosis, the values for creatinine and urea clearance are closely correlated with the number of glomeruli. Maximum specific gravity falls with the decrease in the number of glomeruli until the latter reaches 700,000 to 800,000 per kidney after which it remains fixed in spite of further reduction in the number of glomeruli. If the number of glomeruli per kidney is less than 700,000, the systolic blood pressure is invariably over 150 mm. of mercury. In certain cases of acute infection and jaundice, the clearance and concentrating ability may both be markedly reduced in spite of a normal number of glomeruli showing no significant changes in histologic sections This is also true of toxic nephrosis in dogs poisoned with uranium acetate.

In determining whether the renal lesion in acute nephritis persists or is healed, according to Murphy,23 no one test is reliable as a guide, but a composite picture obtained by several tests may be a fairly accurate prognostic index He points out that (a) the presence of hypertension indicates an active glomerular lesion, (b) albuminuria decreases when healing has taken place, (c) the dilution and concentration test of Volhard is a reliable indication of the progression of the kidney lesion, (d) the blood urea clearance test is considered the most satisfactory but in most cases it has no advantage over the dilution and concentration test, (c) the determination of the sedimentation rate of the erythrocytes is of distinct aid in prognosis. When the renal lesion is becoming quies-

cent, the rate falls and when the lesion is progressing it rises.

Diuresis

In an article on the use of diuretics in Bright's disease, McDonald²⁴ points out that in hemorrhagic nephritis diuretics should not be used. In the active chronic stage the use of digitalis is advised if myocardial insufficiency is present. He believes that the mercurials are of some value in reducing edema, but care should be used to see that the albuminuria and hematuria are not increased by its use and that no mercurialism develops from retention because of reduced renal function. In degenerative Bright's disease where the only pathology is an involvement of the tubules, the potassium salts, especially potassium nitrate, are useful. In this condition the intravenous administration of a hypertonic solution of sugar is, in addition to the diuretic effect which is frequently obtained, valuable as a source of energy. The mercurial diuretics, such as novarsurol and salyrgan, can also be used in this degenerative form of the disease without danger in their administration. In some cases, particularly those associated with a disturbance of calcium metabolism and clinical evidence of tetany, the use of parathyroid extract has given good diuretic response. In renal lesions of vascular origin digitalis, intravenous sugar solutions and salvrgan, either alone or combined with ammonium nitrate, are of distinct value.

Using a mercurial diuretic, esidrone, Volini and Levitt²⁵ observed that the immediate effect of mercurial diuresis is a reduction in the venous blood pressure. This drop in venous pressure is directly proportional to the degree of diuresis. The determinations were carried out on patients with heart failure.

NEPHROSIS

Murphy, Warfield, Grill and Annis²⁶ present a review of 9 cases of genuine lipoid nephrosis studied over a variable period of time. One patient was observed for 15 years, 2 for 12 years, 1 for 7 years, 1 for 5 years, 2 for 2 years, and 1 for 3 months. Two of the patients died and were studied post mortem, 6 recovered completely and 1 is under observation. One of the patients studied post mortem showed no evidence of structural change in the glomeruli. One of the main reasons for making this distinction between lipoid nephrosis and chronic nephritis is that patients with lipoid nephrosis recover while the others usually do not. The disease is identified clinically by certain positive manifestations and by the absence of certain other features found in chronic glomerulonephritis. The positive features are marked albuminuria, hypercholesterolemia, edema, and doubly refracting lipoids in the urine Hypertension, nitrogen retention, genuine uremia and an abnormal number of red blood cells in the urmary sediment are lacking. There are no indications of cardiovascular changes, such as hypertrophy, arteriosclerosis, or albuminuric retinitis. The plasma protein, particularly the plasma albumin, is markedly reduced

After producing a state of hypoproteinemia in dogs by means of a low protein diet, Weech²⁷ found a progressive decrease in the concentration of the albumin in the serum. At first the decline was rapid, later more gradual. A return to an adequate diet of protein depletion resulted in a regeneration of the serum albumin. When the period of protein depletion was short, the regeneration was rapid and the rise of albumin followed a straight line path of concentration until the previous level of health was reached

However, after long and debilitating periods of depletion, the regeneration, although initially rapid, was subsequently retarded and approached the concentration of health very slowly. It is suggested that the delayed type of regeneration results from injury to the mechanism responsible for albumin synthesis, probably the liver.

The observation is made in this connection of damage to the albumin synthesizing mechanism in nephrosis. A case is cited which showed a constant protein level in the serum near 3.9 Gm. per cent even though the diet varied from 68 to 180 Gm. If the hypoproteinemia were due merely to a loss of albumin in the urine a constant serum protein would be difficult to understand.

Concerning the development of edema, Weech, cites the work of Goettsch and Kendall which showed that the albuminglobulin ratio of a transudate is related closely to the albumin-globulin ratio of its corresponding serum. Since the lymph and edema fluid are similar in this respect and there is strong support for the concept that lymph and edema fluid originate by filtration, there is little ground for believing that protein crosses the capillary wall by any other process than that of simple filtration.

In regard to another function of serum albumin, that of maintaining blood volume, the results of Darrow's work indicate that in nephrosis the blood volume and plasma volume are below normal during the edematous stage. Experimentally it is shown that along with the fall in albumin there is a progressive decline in total blood volume. The decline in red cell volume is likewise continuous, but the plasma volume decreases from 20 to 30 days and thereafter remains approximately constant. The rate of decline is more rapid for plasma volume than for cell volume for the first days; therefore,

at this time the red blood cells must appear to rise even though the total quantity is falling.

Weech states that such measurements may lead to the incorrect conclusion that ingestion of a deficiency diet is temporarily beneficial on the hemoglobin and erythrocyte content of the blood. Clinical records may show this fallacy for, as illness and anorexia tend to go hand in hand, so also does failure of the appetite associate itself with a fall in the serum albumin. In regard to the treatment of edema, the results of intravenous injection of blood, serum protein and acacia have been studied. The use of acacia is limited because of reactions. The diuresis which occurs is shown to be the result of an increase of plasma volume since the hematocrit reading fell and the albumin increase was slight, the globulin fraction actually falling enough to produce a decrease in the total protein. Red cells suspended in saline were also found to cause a diuresis.

Dietary measures were studied to determine the relative efficacy of certain proteins in replenishing the serum albumin after a diet, which caused a depletion of serum albumin, had been given. The 6 substances tested were beef serum. egg white, beef chuck, beef liver, casein and gelatin. These were found to be effective in the above order, beef serum and egg white being most potent while the effect of gelatin was negligible. Casein was half as potent as beef serum in restoring serum albumin. These results may be applicable clinically but their effectiveness is limited by the state of the synthesizing mechanism which at times may be depleted.

The relationship of plasma volume and total blood volume to serum albumin concentration, nonprotein nitrogen and the degree of anemia in Bright's disease, was studied by Harris and Gibson ²⁸ It was

found that the plasma volume tends to vary directly with the serum albumin concentration and indirectly with the degree of anemia present. In the edematous stage, hypoproteinemia tends to diminish, and anemia is likely to augment the plasma volume. During diuresis there is a tendency for the plasma to increase The relationship of the changes in plasma and circulating red cell volume is such that the total blood volume always remains below normal. If congestive heart failure is present in chronic nephritis, plasma, circulating red cells and total blood volume are above average levels found at comparable levels of anemia in patients with chronic nephritis but without congestive heart failure As anemia progresses, circulation time does not become faster as it does in primary and secondary anemia and tends to be slower in the edematous stage than in the nonedematous stage.

Farr and Van Slyke²⁹ investigated the relation between plasma protein level and edema in nephrotic children. They made observations on the plasma protein levels in 10 children. It was found that there is a close relation between the presence of edema and the level of plasma albumin in the blood. Edema can be controlled satisfactorily in most instances by simple restriction of salt together with an adequate diet when the plasma albumin level is above 1.2 Gm. per 100 cc. This is decidedly below the critical value of 2.5 Gm for adults.

ESSENTIAL HYPERTENSION

(The Nephroscleroses)

Etiology—Since the work of Goldblatt³⁰ has shown that renal ischemia will produce hypertension, considerable attention has been focused on the kidney as the cause of hypertension in man

Some investigators have attempted to produce hypertension by other means.

Heymans³¹ induced arterial hypertension in dogs by sectioning the cardioaortic and carotid-sinus moderator nerves. The hypertension thus brought about could be maintained for 9 to 26 months. It was found, however, that excision of the sympathetic paravertebral ganglionic chains from the stellate ganglia down to the pelvic ganglia prevents or causes the disappearance of this type of experimental hypertension

By wrapping 1 kidney in cellophane and silk, Page³² produced arterial hypertension. This caused a perinephritis resulting in a thick fibrocollagenous constricting hull Renal ischemia was thus produced by a method different in principle from clamping renal arteries. Removal of the offending kidney or the hull around the kidney or bilateral adrenalectomy abolished the hypertension, but denervation of the renal pedicle did not prevent its development.

The problem of high blood pressure in man with particular reference as to whether it is of nervous or chemical origin is discussed by Pickering 33 In persistent hypertension, the blood flow through the upper extremity seems to be normal; that is to say, the increased perfusing pressure is balanced by increased vascular resistance If the abnormal factor producing vasoconstriction is of nervous origin, removal of the nervous influence should cause a rise in blood flow, for the increased arterial pressure would not be balanced by increased resistance. If, however, the abnormal factor were not nervous in origin, the blood flow would remain normal. It was found that in essential malignant and chronic nephritic hypertension the blood flow remains normal after removal of the vasomotor nervous tone This experiment suggests that the abnormal factor causing an increase in peripheral resistance is not nervous but is presumably chemical in origin.

Keith, Wagener and Barker³⁴ have classified the different types of essential hypertension into 4 groups according to their severity. Group 1 consists of patients with milder hypertension of the benign type which may last for years without causing symptoms. Cardiac and renal functions are adequate and retinal changes are minimal. Group 2 is made up of patients with a high and more sustained hypertension than those of group 1. They are more nervous, but their cardiac and renal function is satisfactory Retinitis is not present, but changes are more marked than those in group 1. In group 3 the hypertension is often high and sustained Though heart and kidney function may be adequate, there are some minor alterations in function referable to these organs There is an angiospastic retinitis with definite sclerotic changes in the arterioles, but edema of the discs is not present. Group 4 includes the cases commonly designated as malignant hypertension. The great majority of these patients dies within a year. The characteristic symptoms are nervousness, asthenia, loss of weight, headache, visual disturbances, dyspnea on exertion and nocturia. The important retinal alteration is edema of the discs. In addition, marked spastic and organic narrowing of the arterioles with diffuse retinitis is present. The histopathologic changes in the arterioles of the pectoralis major were found not to be consistent and no definite correlation between these changes and the division of the cases into 4 groups was observed However, more patients who have marked changes in the arterioles of muscles belong to group 4 and have corresponding changes in the retinal arterioles prognosis in these cases is more serious.

Psychosomatic considerations in essential hypertension are discussed by Palmer,³⁵ who defines psychosomatic medicine as that viewpoint in medicine which attempts to look upon the whole patient; that is, as an individual with a disease, not merely a case that may fit into a pathological classification Heredity is recognized as a factor since hypertension is more common in some families than others. Pseudoheredity or social heredity is another possibility in explaining the high incidence of hypertension, since in some families life is more competitive and the children are "pushed" due to the social and philosophical aims of the parents These habits form patterns that express aggression and thus elevation in blood pressure may become a conditioned response. The parents may be maladiusted and condition the child to fear life and be hostile to it rather than to face it. Early in life he may be educated to be a hyperreactor to certain situations and increased arterial tension will become part of his way of living. These patients may be placed outwardly, but inwardly they are tense, fearful, aggressive, and hostile. This hostility is inhibited, creating a continual state of emotional tension, and a rise in blood pressure results In the management of these patients, the physician should stress the treatment of the person rather than his blood pressure. A discussion of the patient's problems and life trends with the establishment of a lightened work program and frequent provisions for mental relaxation and light physical exercise is better than enforced somatic rest without consideration of psychic tension.

Hoerner, Fontaine and Mandel³⁶ have studied the effect of a persistent hypertension on the kidneys. They induced a permanent arterial hypertension in dogs by section of the internal portion of the vagus nerve (corresponding to

the depressor nerve) and the carotid branch, according to the method of Heymans. The dogs were allowed to carry the hypertension for 2 years, at which time renal function was found to be normal and microscopic studies of the kidney after unilateral nephrectomy showed no lesion that could be attributed to hypertension.

A study of the arterial lesions produced in rabbits by renal artery constriction was made by Wilson and Pickering.37 The acute arterial lesions found in rabbits with severe hypertension are of 2 kinds, namely, acute necrosis and cellular intimal thickening These arterial lesions are structurally identical to those of malignant hypertension described by Fahr. The incidence of the lesions was related to the degree of hypertension but not to its duration The lesions were most frequent and severe in the intestines, but were also found in the stomach, liver, suprarenal, heart, and eye They were absent from the kidney to which the renal artery has been constricted It is suggested that a greatly raised intra-arterial pressure is a chief factor determining these lesions in human and experimental hypertension

Using a modified Goldblatt clamp, Pickering and Prinzmetal³⁸ found that in the rabbit, constriction of 1 renal artery, the other kidney being intact, is sometimes followed by a small and transient rise of blood pressure and usually by atrophy of the ischemic kidney. Constriction of both renal arteries or of the renal artery to the only functioning kidney causes a slow rise of arterial pressure to a level which may nearly double the preoperative value. In such animals the heart is hypertrophied and the degree of hypertrophy seems to have some relation to the degree of hypertension.

De Wesselow and Thomson³⁹ studied the value of potassium and sodium in

the serum of hypertensive patients and those with normal blood pressure. They found that the serum in these cases tends to show a lower level of potassium than that of patients with normal blood pressure on the same diet. This change was especially marked in malignant hypertension. Low levels of serum sodium were not infrequent in malignant hypertension. The giving of sodium salts raised the blood pressure of hypertensive subjects while potassium salts had the opposite effect. These changes in blood pressure were slight. Attempts at depletion of the body sodium were without effect on the blood pressure.

Recent experiments done by Miller and Bruger⁴⁰ showed that patients with essential hypertension and those with a secondary hypertension due to chronic nephritis responded differently to the Hines and Brown cold pressor reaction. The blood pressure response to cold in patients with chronic nephritis is similar to that in normal subjects A hyperreactor response, therefore, in a patient with increased arterial pressure would exclude the possibility of hypertension due to chronic renal disease, but the converse is not true

In any case of essential hypertension, a primary cause should be sought. Nuzum and Dalton⁴¹ report a case and review the literature of secondary hypertension due to a pheochromocytoma, an adrenal tumor. They point out that Cushing's syndrome simulates this condition very closely. The important diagnostic points in pheochromocytoma are paroxysmal hypertension, increasing intolerance to glucose, and roentgenologic evidence of enlargement of the adrenal gland as seen when air is injected into the perirenal area. The signs and symptoms are a feeling that the heart is beating fast, breathlessness, pallor followed by flushing, and sometimes nausea and vomiting

Later, extreme fatigability, tremor and indisposition will develop. There is usually a paroxysm of hypertension and an increase in pulse pressure, but a relatively slight increase in heart rate is noted. Glycosuria may or may not be present and there is a decrease in sugar tolerance. Signs of congestive heart failure may develop. A case is reported in which a diagnosis was made and recovery from the hypertension occurred postoperatively. Autopsies have shown that in 15 to 20 per cent of the cases, the adrenal gland on the side opposite the tumor has functioned inadequately. Hypoadrenalism may occur shortly after operative removal of the tumor and proper therapeutic procedures should be instituted at this time.

Eye Grounds — The prognostic significance of ophthalmoscopic findings in cases of high systolic blood pressure was discussed and classified by Gillan.42 The systolic pressure was selected for study because all observers cannot agree on the exact location of the diastolic pressure and it is easier to refer cases to 1 criterion than to 2. Two points were chosen for special observation: (1) The state of the retinal blood vessels, and (2) the presence of deposits, such as exudates and hemorrhages The classical signs of arterial degeneration were present, namely, burnished copper wire appearance, tortuosity, and irregular caliber of the arteries and deflection and constriction of the veins at the arteriovenous crossings In addition, 2 other features were noted (1) A haze overlying the arteries at points, especially at the arteriovenous crossing and obscuring the vessels wholly or in part; and (2) attenuation of the blood stream to a point of complete obliteration in some cases and of reduction to a mere thread in others The appearance of the vessels was graded as follows.

FIRST DEGREE—Copper wire appearance of arteries only, or normal appearance.

Second Degree—Tortuosity of arteries. Deflection and constriction of veins at arteriovenous crossings.

THIRD DEGREE—Irregular and reduced caliber of arteries

FOURTH DEGREE—Haze overlying the arteries at points and especially at arteriovenous crossings.

FIFTH DEGREE—Marked attenuation of the blood stream, causing threadlike appearance in one or more arteries.

As a general rule, the characteristics of any degree are in addition to those of a preceding degree, but this is not always true. A study of the results of these observations reveals a close relation between the degree of retinal arteriosclerosis and the incidence of cerebral hemorrhage and death. Of those cases exhibiting fifth degree sclerosis, seven-eighths develop signs of cerebral hemorrhage within a period of observation averaging 2½ years One-third of the patients in the groups representing the 3 most severe degrees of retinal arterial degeneration had vascular lesions of the brain during observation. Characteristic exudates were found in 22 of 83 cases These were circular in shape, surrounded by a faint dark halo and were aggregated in the macular area in all except 2 cases (in 1, they were scattered, and in the other they were arranged around the central area of the fundus). Neither exudate nor hemorrhage was found to be of any prognostic significance.

Electrocardiography — Electrocardiographic changes and the cardiac enlargement in essential hypertension show a strong correlation, according to the work of Rasmussen and Thingstad.⁴³ They believe that the electrocardiographic changes described as characteristic of hypertension are due to varying degrees of left ventricular enlargement (dilatation and hypertrophy) and are not caused

by disease of the coronary arteries. Classifying the electrocardiographic changes according to degree into 4 types they found that types 1 and 2 with comparatively small changes in the electrocardiogram corresponded to slight and moderate cardiac enlargement, while patients with gross changes in the electrocardiogram, as in type 3 (left ventricular preponderance), and type 4 (bundle branch block) had the largest hearts. No relation between the degree of cardiac enlargement, electrocardiographic changes and the height of the blood pressure was noted.

Treatment — The results of subdiaphragmatic sympathetic denervation in a series of hypertensive cases reported by Craig and Adson⁴⁴ were as follows Failure, 20 per cent; temporary, 28 per cent; fair, 28 per cent, and good, 24 per To obtain the best results, cases selected for operation must be carefully Mild cases of hypertension chosen (group 1) amenable to medical treatment are not considered Operation seems most efficacious in the definite vasospastic type of hypertension in which sharp and brisk rises in blood pressure occur when the hands are immersed in cold water and in cases in which a marked fall in blood pressure is produced by the administration of pentothal sodium, sodium amytal or a nitrite general, the patient should be under 50 years of age with hypertension classed as of group 2 or 3. Cases with cardiac and renal damage (group 4, advanced cases) are eliminated Contraindications to the operation are congestive heart failure, angina pectoris, marked renal insufficiency and advanced arteriosclerosis

Crile⁴⁵ presents the results of *celiac* ganglionectomy in 35 patients operated upon 2 or more years ago. Of this number, 10 have died, 1 from uremia and the other 9 from cerebral hemorrhage.

The average decrease in blood pressure was 39/20. Symptomatic improvement was seen in 91 per cent of the cases and 81 per cent returned to their normal occupations. The calendar age of the patients has no effect upon the results of celiac ganglionectomy; it is the physiological age, the condition of the blood vessels and the extent of the arteriosclerosis that determines the effectiveness of the surgical procedures for the relief of hypertension Secondary hypertension due to nephritis is not considered a contraindication to operation if the urea clearance test is above 50 per cent.

In another article, Crile⁴⁶ recommends that *decapsulation of the kidney* be done in addition to celiac ganglionectomy for essential hypertension. Although only 6 cases have been done in this manner, he states that it seems to increase the effectiveness of celiac ganglionectomy. In some of the more severe cases in which decapsulation was performed, a decided congestion of the raw surface of the kidney was seen when the capsule was removed.

The multiplicity of methods for surgical relief of hypertension shows their slight value, according to Abrami, Iselin and Wallich ⁴⁷ They attempted to revascularize the kidney by *nephro-omentopexy*, attaching the omentum to the scarified surface of the decapsulated kidney. This was done in 2 cases and, although the procedure failed because the operation was performed too late, they concluded that this method of relieving renal hypertension is possible in the human being

An interesting observation concerning the surgical relief of essential hypertension was made by Volini and Flaxman,⁴⁸ who studied 27 hypertensive cases on whom nonspecific operations were done They found that symptomatic relief and reduction in blood pressure resulting

from these nonspecific surgical measures are similar and sometimes better than those obtained by specific procedures for the relief of hypertension. The average duration of the symptom-free stage was $3\frac{1}{2}$ years.

As a result of an investigation of 100 patients diagnosed as having hypertension not due to glomerulonephritis, Harrison and Williams⁴⁹ suggest an approach to the problem of hypertension by urologic methods. This may be beneficial to many patients and lead to cure in some. Evidence of some disorder of the urinary tract was found in 30 of their 100 patients and in most of these cases the urinary tract disease antedated the hypertension

The pharmacological action and clinical effects of tincture of crataegus made from whole fruits of hawthorn (Craetaegus oxycantha) were investigated by Graham ⁵⁰ In cases of auricular fibrillation and mitral stenosis with failure the drug was ineffective, and the patients subsequently improved when digitalis was administered. However, in every case of hypertension, both of the essential and chronic nephritic type, both the systolic and diastolic pressure were reduced. After discontinuing the drug, the blood pressure returned to its previous high level within 2 weeks.

Evans and Loughnan⁵¹ tested the effect of 33 drug preparations on the blood pressure and symptoms of 70 patients with hypertension. It was found that none of the preparations produced any hypotensive effect. Only 6 of the drugs, bismuth subnitrite, iodine and iodide, bromide, sodium luminal, theominal and potassium thiocyanate relieved symptoms more than did the placebo

The use of the thiocyanates has been discussed by Wald, Lindberg and Barker.⁵² They divided the toxic manifestations into those present when the blood

level is 8 to 14 mg. (the level at which the hypotensive effect of the drug is fully effective) and those which occur when the blood level exceeds these lim-The commonest manifestations in the first group are weakness, fatigue and aching and cramping in the muscles of the calf. These symptoms are often transitory and disappear after 2 to 6 weeks of medication. Toxic dermatitis manifested by a maculopapular, itching, scaley eruption occurred in only 6 cases and was never serious. Severe exfoliating dermatitis was not encountered and reported cases may be the result of excessive dosage. After long continued administration of the drug a benign enlargement of the thyroid gland may occur, but the basal metabolic rate is not increased and the condition is improved when thyroid is administered. Mild gastrointestinal disturbances consisting of pyrosis, abdominal discomfort, anorexia, nausea and vomiting may occur at the usual therapeutic levels.

Above therapeutic levels, nausea and vomiting are among the first signs of thiocyanate toxicity Severe diarrhea, abdominal pain and cramping may occur independently or as part of a general extreme toxic state. The signs of toxicity of the second group are seen only in the presence of high blood levels Vascular collapse may or may not be associated with the other major toxic reactions Cerebral thromboses are probably not toxic effects but are secondary to the severe vascular insufficiency resulting from a sudden and marked depression of arterial tension Cerebral manifestations of toxic origin appear as a rule when the blood level has reached 20 mg or more per 100 cc of blood The earliest sign is that of slurring speech associated with word aphasia Later marked confusion and even delirium develop. The authors believe that

no patient who previously experienced angina suffered to a greater degree from this symptom during the administration of thiocyanate.

In several elderly patients with severe grades of progressive vascular disease and hypertension who were plethoric and obese with good muscular development at the beginning of thiocyanate treatment, anemia, emaciation and muscular wasting developed after 5 to 10 years of constant therapy. This may be due to a progressive vascular breakdown in hypertensive patients who might have died of heart failure or a cerebral or coronary accident years later if they had not been treated In younger patients with a more elastic hypertension this progressive breakdown does not seem to occur.

The mode of action of sodium sulfocyanate in reducing hypertension is discussed by Doles 53 In a previous article⁵⁴ he showed that when the hypertension is due to a macrocytosis the pressure returns to normal on an adequate diet of red meats and sufficient sodium sulfocyanate to reduce the red cells to normal size. If the hypertension results from macrocytosis and arteriosclerosis the improvement is in proportion to a reduction in the size of the red cells, and in the group where the hypertension is due to arteriosclerosis without evidence of macrocytosis, no reduction in blood pressure occurred

Doles pointed out in 1935 that in some patients with hypertension due to enlarged red blood cells the pressure becomes normal on a diet adequate in red meats and a daily intake of iron not exceeding 10 mg. Later it was found that those patients who did not respond to this treatment needed a minimum intake of iron of only 3 to 5 mg. to provide for their needs. This was evidence that

the cells were using iron stored somewhere other than in the bone marrow.

Quantitative studies on the iron content of viscera of hypertensive patients who had died revealed a normal iron content of bone marrow but the liver and spleen showed an iron content of 150 mg. per 100 Gm. of tissue. Some means of precipitating this iron was desired, and since sulfocyanates are employed commercially to precipitate iron in certain materials, this drug was used. Ten patients with hypertension and macrocytosis were placed on a general diet and quantitative determinations were made for iron in the urine and stools. A diet low in iron was given and the iron content of the stools and urine was markedly reduced. Continuing this same diet the patients were given 3 drams (12 cc.) of sodium sulfoncyanate solution (20 grains to 1 ounce-1.3 Gm. to 30 cc) twice a day and the iron content of the stools and urine was found to be increased.

Contraindications to the use of sulfocyanates are hypertension in which the cells are normocytic normochromic, normocytic hypochronic, microcytic normochromic, microcytic hypochromic, and cases with macrocytic hypertension showing an increase in the icterus index of 7 units or more without liver disease This latter type is in the pernicious anemia group and will respond to liver parenterally. The dose of sodium sulfocyanate recommended is 1 gram (006 Gm) twice a day for 1 week, increased to 2 grains (013 Gm) twice daily if there are no untoward symptoms. If no improvement occurs, this dose may be increased to 71/2 grains (0.5 Gm.) a day, providing toleration is good.

Friend and Robinson⁵⁵ describe the results of experiments done to determine the action of sodium thiocyanate upon

tissue oxygen consumption. They found that oxygen consumption of rat liver cells is depressed by the thiocyanate ion added to serum in vitro, but the limiting concentrations with their method was between 20 and 30 mg. of the drug per 100 cc. of blood. Serums from patients receiving thiocyanate with blood concentrations of the drug ranging between 8 and 22 mg. per 100 cc. did not appear to depress the oxygen consumption of rat liver suspended in them.

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METABOLISM, DISEASES OF

By Joseph T. Beardwood, Jr., A.B., M.D.

OBESITY

Etiology—The debate of the rôle of endocrine glands versus excess diet in obesity still rages. E. W. Hancock1 reports his observation on a series of obese children and adults and points out that while most endocrinologists stoutly maintain that obesity is nearly always endogenous, in giving endocrine therapy they put the patient on a reduction diet and that those who follow the school of thought which blames hyperalimentation usually give a little thyroid to aid their reduction diet. The author feels that the direct relationship of obesity to any endocrine gland has not been proven nor has any adiposogenic hormone been detected. He proposes that a carefully constructed diet be used with a thyroid adjuvant, realizing that the use of the latter is entirely empiric He feels that this enables one to keep the patient possibly under closer observation than if diet alone were used He frowns upon exercise as a great aid to reduction, since it offsets any benefit gained by increasing the appetite. He feels that fluid and salt restriction is of no lasting value

J. A Greene² reports observation on 350 cases of obesity in which sufficient data were available regarding the food intake and activity during the gain in body weight in 154 cases. Gain in weight was associated with pregnancy or pregnancies without a history of increase in food intake or diminished activity in 32 instances. Most of these patients gained from 15 to 25 pounds with each pregnancy, maintained the added weight, and thus became obese after from 3 to 6 pregnancies. There were 13 patients who were either always obese or became obese without history of change in activity or

food intake. The gain in body weight which occurred simultaneously with diminished activity in 104 cases was accounted for in 5 instances by change in occupation and in 99 by a long illness. disability, or convalescence. Of 300 women, sufficient data regarding menstruation were available for 289. The menses of 143 were normal. Forty-eight had passed the menopause, but the obesity began several years prior to the menopause and the menses had been normal during that time. Ovarian dysfunction could be excluded as an etiologic factor in the adiposity in 191 cases. Obesity began before puberty in 5 cases, but menstruation was normal. Adiposity began after the menopause in 15 instances and antedated it in 2. Menstruation was irregular in 34 cases, absent in 13, scanty in 5, painful in 7 and excessive in 7. Although the incidence of obesity in myxedema, pituitary tumor, chronic encephalitis, suprasellar tumor and diabetes insipidus is high, it was present in most cases before the onset of the other malady. Patients with myxedema, pituitary tumor or chronic encephalitis became either more or less obese, that 15, as many patients lost weight as gained weight after the onset of myxedema and pituitary tumor, and loss of weight was 5 times more prevalent than gain in weight after the onset of chronic encephalitis Low Caloric diets were known to have been followed for an adequate time by 146 patients, and all of them lost body weight satisfactorily The patients who lost weight on low Caloric diets included those who had various menstrual disturbances. those who became corpulent with pregnancy, illness, operation, myxedema, pituitary tumor, chronic encephalitis and increased food intake. Adiposity developed in association with 36 different diseases or disabilities in the patients known to have lost weight satisfactorily. Inactivity occurred simultaneously with gain in body weight in 67.5 per cent. A history of an increase in food intake was obtained in only 3.2 per cent.

DIABETES

Diagnosis—Matthews, Magath and Berkson³ report experiences at the Mayo Clinic with the 1-hour 2-dose tolerance test which was first composed by Dr. Exton in 1931. This test is based on Allen's paradoxical law of dextrose utilization.

Following an overnight fast, samples of blood and urine are collected and one-half of a solution of 100 grams dextrose in 650 cc water is given by mouth. Thirty minutes after the ingestion of this solution a second sample of blood is collected and the second dose of the dextrose solution is given. Thirty minutes after the ingestion of the second dose a third sample of blood and urine is taken The authors of this article draw the following conclusions:

- 1. Advancing age produces a progressive elevation of the blood sugar level at every phase of the blood sugar time curve obtained with the dextrose tolerance test of Exton and Rose. The degree of this, however, is insufficient to invalidate conclusions 2 and 3
- 2. A fasting blood sugar that exceeds 120 mg per 100 cc of blood is diagnostic of diabetes. This value, however, was exceeded by only 21 per cent of the persons with diabetes in this series of cases in which diabetes was minimal. In contrast, no person in whom the carbohydrate tolerance was considered normal.

had a fasting blood sugar that exceeded 110 mg.

3. According to their experience, the most effective criterion, with the Exton-Rose procedure, for differentiating persons suffering from diabetes and normal persons is the hour value of the blood sugar. If 158 mg. per 100 cc of blood is taken as the critical level so that individuals showing a blood sugar reading below this level at the hour are designated nondiabetic and individuals with readings at or above this value are designated presumptively diabetic, a high percentage of correct diagnoses can be expected. As far as the observations of this series are concerned, all individuals with values at the hour less than 154 mg. were found to be normal, and all individuals with values at the hour of 180 mg or more were found to be diabetic. Hence, these 2 groupings are most definite. Individuals with values at the hour between 158 and 179 mg, inclusive, constituted only a small fraction of their cases (6, or 5.1 per cent, of 117 patients considered to be nondiabetic and 19, or 7.7 per cent of 247 patients considered to have latent or mildest diabetes). The number of cases with a doubtful laboratory diagnosis was smaller by this criterion than by any other criterion applied to the results of the Exton-Rose test. It also was smaller than that obtained by any criteria applied to the interpretation of other oral tests for dextrose tolerance with which they have had experience.

Insulin—The use of protamine zinc insulin is so well established and has been so thoroughly covered by previous articles that it would seem superfluous to attempt to extract the voluminous literature confirmatory of these previous observations. With the use of protamine zinc insulin it is often difficult to avoid postprandial glycosuria and there seems

to be an opinion on the part of most workers that it is ofttimes impossible to have the urine sugar-free for the entire 24-hour period.^{4, 5}

Rabinowitch⁶ attempts to explain why this is true. He points out that in many of his cases it was quite possible to increase the carbohydrate content of the diet as much as 50 Gm. a day without noticing any marked increase in the amount of glycosuria and that his patients would come with a normal fasting blood sugar. He feels that, as these patients seem to go along maintaining an ideal body weight, are able to keep up with their activities and feel well, such a loss is not a serious matter. He feels that from his observations, possibly there may be some relationship between the height of the blood cholesterol and the tendency to develop glycosuria.

It is the thought of the editor of this section that while occasionally transient and mild glycosuria may not be considered a serious matter, it is a thing to be avoided if possible. One should be sure that the blood sugar of these patients is well controlled if glycosuria is allowed to exist, for frequently it is the patient who is spilling small amounts of sugar with slight elevation of the blood sugar who so often develops the various complications of this disease

Crystalline Insulin—Crystalline insulin, "solution of insulin crystals" first developed by Dr. Savhun in 1935, has been studied by Marble and Vartiainen and they conclude that in comparison with amorphous or regular insulin (a) the fall in blood sugar is identical with the 2 preparations so that both must be regarded as rapid acting insulins (b) that while with experimental animals there may be no prolongation with the crystalline insulin, in diabetic patients there is a definite prolongation of the action and that in at least 1 case the

crystalline insulin reached its low peak and returned to the value before injection at 14 hours, and (c) they advanced the thought that possibly to avoid confusion regular insulin should be done away with and crystalline insulin substituted.

Diabetes in Children — Grishaw. West, and Smith⁸ report their observations on a series of 341 diabetic children seen between April, 1920, and January. 1938. The earliest onset of the disease was at the age of 8 weeks, only 4 children of this group were under 1 year when the diabetes was discovered. The sex incidence was almost equally divided. The peak of onset for the entire group occurred between the ages of 11 and 12, and the next highest between 7 and 8 years. They were able to obtain a fam-1ly history of diabetes in 110 cases. The present status of 315 of these children is known Fifty-five of them have died, a mortality rate of 161. Insulin was first available to these patients in November, 1922 Prior to that 25 of the children were seen, 16 of whom are known to be dead Eight of those who died did so within 1 month after the onset of the disease Of the children receiving insulin there is a known mortality of 132 per cent with a duration of diabetes in this group from 2 days to over 14 years. Of particular interest are the 86 children in whom diabetes developed prior to January, 1928, and who theoretically had an opportunity to live 10 years or more; 25 per cent of these died, only 3 deaths occurring within the last 8 years.

Inquiry into the causes of death in this entire group shows that 61.8 per cent of the deaths must be attributed directly to diabetes. The highest mortality was in the group treated before insulin was available, in which 79 per cent died as a result of diabetes. In the

group of patients living at the time the article was written (260) 86 per cent have had diabetes for 2 years or longer and the longest duration was 17 years and 7 months. In evaluating this present group it is interesting to see that 73 children have survived coma, 33 on more than 1 occasion One child had been admitted to the hospital 21 times in coma; this patient is now married and has a daughter 3 years of age. Retinitis was observed in 2 cases, cataracts in 1. Incidence of tuberculosis was remarkably low. It is interesting to know that in this group there were 18 pregnancies in 12 women, and there has been no maternal mortality in this group.

Ophthalmological Manifestations of Diabetes—Smith⁹ discusses some of the ocular manifestations of diabetes One of the rarer manifestations is that of lipemia retinalis Moore of London states that he has not seen such a case since the introduction of insulin. Retrobulbar neuritis is usually found in older persons. is characterized by a small central scotoma and usually responds to treatment. If the condition is allowed to progress there may be some resulting atrophy. Iritis demonstrates the lack of resistance to infection which diabetic patients show There are more often changes in the pigment cells on the posterior surface of the iris They become swollen, thus throwing the iris into more prominent folds The cells often become detached and may be found on the anterior surface of the lens.

Most so-called diabetic cataracts are nothing more than ordinary senile cataracts developing in patients with diabetes. The true diabetic cataract is found in young persons, is bilateral and develops rapidly. It is characterized by flaky lesions which develop faster in the posterior layers of the cortex. Senile cataracts tend

to develop earlier in diabetic than in nondiabetic persons.

Likewise retinitis is somewhat similar in that in the vast majority of cases in which it develops there is usually associated a raised blood pressure, vascular disease and albumin in the urine. Often it is difficult to state from ophthalmoscopic appearances whether a given case of retinitis is due to diabetes, nephritis or arteriosclerosis. Wolfe states that there are certain characteristics of a true diabetic retinitis, (1) it rarely occurs in a young subject, (2) the patches of retinal exudate tend to have sharply defined edges, are distributed in an irregular manner and sometimes form an irregular ring around the macular region, (3) small dark round retinal hemorrhages are suggestive of diabetes. As such they lie in the deeper layers of the retina.

With regard to prognosis, Nettleship found that of 48 patients with diabetic retinitis, 60 per cent lived for more than 2 years. Thus, it is an indication of some gravity but is not as serious a sign as retinitis in renal disease.

Hemorrhage is more apt to follow surgery of the eye in a diabetic than in a nondiabetic person. Changes in refraction are common The exact mechanism for this is not known, but it may be due to an alteration of the osmotic pressure in the aqueous humor. This in turn causes an altered index of refraction of the lens cortex. It may cause myopia in some cases while in others hyperopia may develop. It may appear shortly after the beginning of insulin therapy. The author cites such cases.

Bucklers¹⁰ describes his observations in a case in which changes in the lenticular turbidity were recorded continuously and metabolic tests were made simultaneously. A tabular report indicates the gradual retrogression of the

cataract, the sugar content of the urine and blood, the specific gravity of the urine, the water balance and the dose of insulin that was administered. The retrogression of the turbidity of the lens began in the axis and advanced in an irregular manner toward the periphery, but it seemed to be more rapid on the temporal side. The table discloses that the subsidence of the turbidity was already noticeable at a time at which there still existed a considerable metabolic disturbance.

One increase in the blood sugar was accompanied by a slight increase in the turbidity of the lens, but a second increase in the sugar content caused no lenticular changes. It cannot be decided whether the decrease in the visual acuity was caused by a lenticular turbidity or by a change in the refractive power during the temporary hyperopia. The author believes that the 2 processes developed simultaneously. In trying to find an explanation for these 2 disorders, the author cites the theory advanced by Granstrom for the development of the diabetic impairment in the refraction and the one advanced by Braun for the pathogenesis of the lenticular turbidities Both of these authors ascribe great importance to the disturbance in the mineral and water exchanges. The turbidity in the lens as well as the transitory hyperopia are apparently due to a temporary increase in the water content of the lens

Diabetes and Hyperthyroidism—Foster and Lowrie¹¹ report the observation of coexistence of hyperthyroidism and diabetes which is very important because of the fact, as they point out, that many cases are overlooked. They state that certain features during the course of the illness arouse suspicion that thyroid disease may be a complicating factor. An inability to control the

blood sugar and glycosuria with what seems to be a suitable diet and insulin dosage or the failure of a patient to hold his weight or to gain while consuming a diet adequate for either circumstance is significant. These patients also are prone to develop acidosis, especially if they are losing weight or are undernourished. A rapid pulse, intolerance to heat or bedclothes, restlessness, flushing, apprehension, a moist skin and eye signs are all aids to a correct diagnosis, particularly in the younger patient.

Forty-two cases of diabetes associated with hyperthyroidism were found in the admissions to the Henry Ford Hospital from 1925 to 1938. During this period there were 214,223 new cases examined. Diabetes was present in 1616 of these and a total of 1607 operations for hyperthyroidism was done. Nine patients have died They had an average survival period of 4 years and 1 month Vascular disease was a primary or complicating factor in all the deaths. Toxic adenoma was present in 6 Evidence is presented which would indicate that following thyroidectomy the carbohydrate metabolism was improved. The authors believe that the diagnosis of hyperthyroidism as a complication of diabetes mellitus is being overlooked When hyperthyroidism is complicating diabetes mellitus, thyroidectomy is indicated Vascular disease assocrated with hypertension, since insulin has been available, constitutes the major cause of death in this group Acidosis is common but can be successfully combated by a high carbohydrate diet and adequate insulin.

Diabetes and Pregnancy — Smyth and Olney¹² report their observations on 19 infants born to women whose pregnancy was complicated by diabetes. In 14 of the mothers glycosuria appeared only with gestation and was controlled by diet or by a diet and temporary use

of insulin, which suggests glycosuria from causes other than diabetes mellitus. Of the entire group, 11 gave birth to excessively large infants. The infant's blood sugar, even allowing for the effect of predelivery insulin, may be low. The cord blood sugar may anticipate this finding by showing a much lower level than that of the maternal blood taken simultaneously. In 2 of the infants projectile vomiting and cyanosis were striking features, quite possibly related to persistent hypoglycemia. This interpretation circumvented pyloroplasty, which was suggested for 1 of the infants The use of subcutaneous dextrose appeared extremely valuable in carrying the infants through a critical period, after which an apparent adjustment was made.

A follow-up of 1 patient showed a hyperinsulin-like sugar curve at 4 years of age. Reports of post-mortem studies of infants born of diabetic mothers vary. In some no hyperplasia of islet tissue has been found, and the hypoglycemia must be considered functional in type. In others the finding of hypertrophy and hyperplasia of the islets of Langerhans makes the correlation obvious. The relative macrosomia, advanced bone age and more mature genital tract suggest a pituitary effect Complete endocrine pathologic study is reported but the interrelationship is best described as dysfunction Perhaps some interrelationship will be found to account for the mild as well as the fatal hypoglycemia of the newborn infant. Fetal glycogen storage hypertrophy also is postulated as a possible cause for some of the pathologic signs.

Anacidity—Fenz¹³ points out that the relations between the gastric secretion and the diabetic disturbance in the metabolism have been repeatedly investigated in recent years and it was found that, whereas hypoglycemia is usually accompanied by an increase in the hydrochloric acid content, hyperglycemia is accompanied by a decrease. In view of the great significance of the diabetic inhibition of acidity and of its relation to insulinization, the author studied the gastric secretion of 116 unselected cases of diabetes mellitus with the aid of the caffeine test breakfast. He detected anacidity in 65 (56.3 per cent), hypoacidity in 20 (17.2 per cent) and normal acidity or hyperacidity in the others.

That insulinization cannot be the cause of the frequent anacidity was proved by the fact that anacidity was more frequent in untreated diabetic patients than in those who had received insulin; even quite new cases often showed complete anacidity When insulin was administered during the caffeine test breakfast, the acidity curve increased in patients with normal acidity and hypoacidity, especially when a hypoglycemic shock resulted Diabetic patients who readily respond to insulin are more often subject to anacidity than are those who are resistant to insulin, but the latter show hyperacidity more often than do those who are sensitive to insulin. The severity of the diabetes does not determine the appearance of a diabetic anacidity It was found that 44 of the 116 patients had the typical diabetic diarrheas. The fact that 70.5 per cent of those with diarrhea had anacidity and that among those with severe diarrhea the percentage of anacidity reached 78 seems to indicate that the diabetic diarrheas can be regarded and should be treated as gastrogenic diarrheas Discussing the causes of diabetic anacidity, the author suggests that deviations in the relationship between insulin and counter-regulation, to the disadvantage of insulin, probably play a part.

Trauma in Diabetes—The relation of trauma to the onset of diabetes is of

interest medically as well as legally and it is of great interest, possibly because the editor concurs so heartily, to read the article of Thomsen14 in which he thoroughly covers the subject of trauma and diabetes. It is pointed out that the conceptions of the causal relation of trauma and diabetes have been increasingly subjected to criticism and scepticism. The author has studied the influence of trauma on the carbohydrate metabolism of 144 nondiabetic individuals and has reviewed and tabulated 81 cases of reported traumatic diabetes. The findings and clinical course in this material are evaluated on the basis of a series of questions which had been formulated by Noorden in the belief that the answers thereto would throw some light on the relation of trauma and diabetes.

The author emphasizes the following viewpoints, most of which are at variance with hitherto prevailing opinions. "If physical traumata—with the exception of direct pancreas trauma-are at all able to provoke diabetes, this property must be attributed to every trauma regardless of its kind and location. In human beings were found neither experimental nor clinical clues justifying the assumption that the posttraumatic sympathicogenous disturbances in the carbohydrate metabolism can lead to diabetes Since a physical trauma can only give rise to a temporary exacerbation of existing diabetes, it can not be thought to 'activate,' i e , bring about, a permanent exacerbation of latent diabetes. It is admitted that the trauma, if the sympathicogenous disturbance in the carbohydrate metabolism depending on it is added to the existing pancreatogenous disturbance, can give rise to temporary glycosuria and, thus make it possible to diagnose an existing latent diabetes It is demonstrated that the claim involving the acknowledgment of a diabetes

as being traumatic, namely, that the patient has not previously presented any diabetic symptoms, is sufficient. Traumatic diabetes after a direct, severe pancreatic lesion is acknowledged as a theoretic possibility."

Although the author admits in theory that diabetes may appear as a direct sequel to a pancreatic injury causing extensive destruction, he believes that other physical traumas are unable to cause diabetes. An injury may cause an exacerbation of existing diabetes, but the exacerbation that occurs immediately after the trauma is only temporary. The frequent assertion that an injury can exacerbate a latent diabetes and make it manifest cannot be maintained.

It probably is not untimely to state that similar conclusions were expressed by Joslin, Root, and Marble in a chapter of Brahdy and Kahn's book, "Trauma and Disease" published in 1937 by Lea and Febiger.

Cardiac Disturbances in Diabetes —Hegglin¹⁵ investigated whether there are connections between diabetes mellitus and cardiac disturbances and what effects insulin exerts on the heart studies were made at the medical clinic of the University of Zurich. He found that the combination of diabetes mellitus and heart disease is comparatively frequent The heart does not escape the general damage that is produced in the organism by the severe metabolic disturbance To be sure, this applies chiefly to aged persons with diabetes. Whether heart disease and particularly coronary sclerosis develops also on the basis of juvenile diabetes, the author is unable to state.

The administration of large doses of insulin to aged persons with diabetes results in impairment of the cardiac function. This does not imply that insulin is harmful also when given in small

doses. Although in a few cases electrocardiographic changes were observed even after small doses, there never was a severe cardiac impairment, especially a cardiac infarct. In the cases in which cardiac infarct and diabetes concurred, no insulin treatment had preceded the development of the infarct.

On the other hand, the large doses of insulin which are required for the treatment of diabetic coma may produce severe myocardial damage. For this reason, aged persons with diabetes must be kept under close observation in order to avoid coma and its circulatory complications. By means of electrocardiographic studies it was possible to determine that a circulatory weakness during diabetic coma is chiefly due to a myocardial weakness; that is, it is not only of peripheral but also of cardiac origin. Consequently, the therapy of the circulatory weakness must attempt to strengthen the heart by strophanthin and to counteract the peripheral insufficiency with the usual remedies. Moreover, it is important to avoid an additional myocardial impairment by insulin; the quantity of insulin should be just enough to counteract the acidotic disorder of the metabolism but a hypoglycemia should be avoided.

Surgery in Diabetes—H. J John¹⁶ states that since the use of insulin in the care of diabetic patients, the surgical mortality rates in this type of case have decreased tremendously. An average of a series of 1767 cases reported before the advent of insulin showed a mortality rate of 20.6 per cent while in 9513 cases reported since 1923, the mortality has been only 67 per cent. There are still tremendous variations in the results reported. These range from 12 to 68 per cent.

Surgery in diabetic patients carries a greater than normal risk, not because

of the diabetes *per se*, but because of obesity, arteriosclerosis, advanced age, and the dangers of infection.

Cholecystitis is common among diabetic patients, and the removal of the gall-bladder usually improves the diabetic condition.

Surgery of the extremities for gangrene is a special problem encountered in diabetes. The best treatment for gangrene is prevention, since the mortality rate in this type of operation is necessarily high, because of the advanced age of the patients and the shock occasioned by amputation.

The proper care of a diabetic patient who has an operation demands the combined services of an internist and surgeon who are interested in the disease. The best results are obtained where there is the best team work.

The most important diagnostic problems encountered in connection with surgery on diabetic patients are: (1) The differentiation between acute appendicitis and acidosis; and (2) the proper diagnosis of unconsciousness which may appear following an operation The latter may be caused by surgical shock, diabetic coma, hypoglycemia, or alkalosis The history and blood chemistry findings are important in making the differentiation from acute appendicitis

Except in situations that present an emergency, a diabetic patient should be subjected to thorough study before any surgical procedure is attempted. The proper dosage and distribution of insulin must be determined if the diabetic condition is to be kept under control satisfactorily after the operation.

The choice of anesthesia is very important. Chloroform should never be used; ether has a great many hazards. The anesthetics of choice when local or spinal anesthesia cannot be used are

nitrous oxide, ethylene, and cyclopropane.

After an operation, the condition of the diabetic patient must be followed most carefully with repeated determinations of the blood sugar, and adjustment of the insulin dosage, so that both hyperglycemia and hypoglycemia may be prevented. Intravenous administration of glucose solutions may be resorted to, provided the injections are accompanied by appropriate doses of insulin.

Newer Physiology of Diabetes-One of the most important contributions to the newer physiology of diabetes is that of F G. Young 17 He reports his experimental work in producing diabetes and the relationship of diabetes to the anterior hypophysis A few years ago the theories on the causation of diabetes mellitus seemed quite complete Within the past 6 or 7 years, however, experimental work on the anterior lobe of the pituitary gland has revealed facts which are very disturbing to the older theories In 1931. Houssay showed that the administration of substance from the anterior lobe of the pituitary from hypophysectomized and depancreatomized animals resulted in a very marked increase in the severity of diabetic symptoms. The author confirms this work and discusses at considerable length the possible nature of this "diabetogenic" material and the possible modes of its action

Dogs were used in Young's series of experiments because they give more consistent results. The pancreas and pituitary glands had not been removed from them as in the animals used in Houssay's experiments. In from 3 to 4 days following the daily intraperitoneal injection of a suitable amount of crude saline extracts of fresh anterior pituitary gland, the urine increased in quantity

and glycosuria and ketonuria supervened. When the same quantity of extract was continued, the animals lost their diabetic characteristics, but when the quantity was increased the diabetic qualities again became manifest. When this process was continued sufficiently long, the majority of the dogs became permanently diabetic, with the exception that they were able to maintain body weight and did not require the use of insulin.

In his evaluation of this work, the author discusses the influence of the anterior lobe of the pituitary gland on the action of insulin, on the islet tissues of the pancreas, on the glycogen stores during a fast, and the influence of the pituitary extracts on ketogenesis. It has been shown that the daily administration of extracts from the anterior lobe of the pituitary gland will markedly lower the hypoglycemic action in rabbits, and that this action is due to a substance which is present in preparations of the so-called lactogenic hormone (prolactin) The author refers to this as "glycotrophic substance" The injection of this glycotrophic substance definitely decreases the tendency of insulin to increase the liver glycogen level, and inhibits the action of insulin in the peripheral tissues

It has been shown that the injection of such diabetogenic extracts will result in a true hypertrophy of the islet cells of the pancreas in several types of animals. The fraction that causes this action has not yet been isolated

With regard to the action on the glycogen stores during a fast, it was found that the administration of glycotrophic substance resulted in a definite increase in the liver glycogen content. The reason for this is not at all clear, and it is suggested that there may be

less utilization of carbohydrates, or that there might be some glycogenesis from fat.

The administration of substance from the anterior lobe will result in an increase in ketone excretion, though as yet little is known of the nature of the active principle which causes such an increase.

In his discussion of the nature of the diabetogenic factor of the anterior lobe of the pituitary gland, the author points out that at least 3 factors are necessary for the production of diabetes in the normal dog. The exact nature of these factors is not known at the present time In referring to the mechanism of the diabetogenic action of the anterior lobe extracts the author states. "inherent processes of manufacture of sugar in the liver and utilization in the peripheral tissues probably exist, these processes being intrinsic properties of the relevant tissues; the precise mutual adjustment of the rates of these 2 processes is mediated by the endocrine system, the antagonistic actions of insulin and the pituitary factors playing an important rôle in this adjustment. If this is so, then freedom from diabetes is the result of a precise regulation of the relative potencies of the pancreatic and pituitary factors. If, for any reason, the regulation is faulty so that pituitary effects predominate, then diabetes may result"

Diabetes and Tuberculosis — El-wood¹⁸ gives the results of collapse therapy for pulmonary tuberculosis and the use of the newer insulins for the control of concomitant diabetes in 21 cases. Despite the limitations imposed on the successful continuance of artificial pneumothorax, the employment of this type of therapy restored more than 3 times as many to health as did elected or enforced rest. The percentage of effective

pneumothorax obtained parallels the results observed in nondiabetic persons. Protamine zinc insulin utilized in all stages of both diseases was as applicable as insulin. It revealed limited advantages in these cases over insulin in the progressive phases of tuberculosis, greater adaptability and better management in tuberculosis therapeutically controlled or regressing. It is of greatest use in diabetes and arrested pulmonary tuberculosis and its advantages in these cases over insulin are comparable to those noted in otherwise uncomplicated diabetes. In terminal pulmonary disease it has little or no advantage over insulin in the control of the diabetic derangement.

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NEUROLOGY

Edited by BERNARD J. ALPERS, M.D.

BRAIN ABSCESS

By ROBERT A. GROFF, M.D.

Alpers¹¹ studied 27 cases which included a histological correlation of the clinical features with the pathological findings. He disclosed the following important facts:

The formation of the wall of the abscess is dependent on the following variable factors: (1) The nature of the invading organism. Some organisms favor wall formation. (2) The resistance of the host. This factor is an intangible element, and, therefore, not easily measured or evaluated. However, the more resistance the organism meets, the more likelihood there is of wall formation.

Time Factor—Alpers found that an abscess of 3 days duration showed no capsule; 1 of 6 days, beginning encapsulation; 1 of 10 days, no signs of capsule; 1 of 14 days, good capsule formation In 12 cases good capsule was present where the history extended over a period of 3 weeks to 11 months One abscess of 2 months duration had a very poor capsule and another of 21/2 months had no sign of capsule formation. The author concludes from these data that the older the abscess, the greater the possibility of encapsulation, but factors such as virulence of the organism and resistance of the host are important determinants for encapsulation.

Relationship of Organism to Encapsulation—The staphylococcus is accompanied by poor capsule formation. Other authors have observed the reverse to be true Cocci are said to favor encapsulation, and the anaerobic group is said to favor encephalitis without formation

of a capsule. A virulent organism, in the blood stream, will cause death before an adequate capsule can be formed. Abscess of the brain is more frequently a complication of chronic than of acute otitis media or mastoiditis. Abscesses with mixed infection do not form capsules as well as those due to a single organism

Most abscesses contain virulent bacteria and rarely is an abscess sterile. This finding is intimately associated with the occurrence of encephalitis about the wall of the abscess. Even abscesses of long standing are sometimes associated with an active encephalitis

Pathology of Capsule—The capsule is composed largely of connective tissue. Alpers did not find evidence of neuroglial elements in the capsule and ghosis was not observed even in the surrounding brain tissue except in a few cases of chronic abscess. The capsule, therefore, is derived from the blood vessels, lymphocytes, and the dura and pia mater. These observations disagree with those of other writers who report neuroglia-fibrils in the capsule.

Treatment of Encapsulated Abscess of the Brain—E A Kahn¹² has presented a very interesting article upon the treatment of encapsulated brain abscess.

A cranial defect is made over the most superficial aspect of the abscess. The dura is opened and the abscess is drained by a dull exploring cannula. About 1½ drams (6 cc.) of colloidal thorium dioxide are instilled. By taking periodic roent-genograms, one can follow the course of

the abscess. Kahn has shown diagrammatically that the abscess migrates to the surface, and in 1 of his patients the abscess delivered itself completely. In those abscesses in which no migration takes place, Kahn removes the overlying cortex, excises the dome, and sutures the capsule to the galea of the scalp.

The ability to visualize the abscess is undoubtedly a step forward in its treatment. The opaque material is phagocytosed by the cellular elements of the capsule so that increase in size of the abscess is demonstrable, even though the pus and the contrast medium do not mix freely. The advantages, according to Kahn, are the ability to visualize the abscess if the abscess is treated by enucleation, and the ability to find the abscess if repeated tappings are used

BRAIN TUMORS

Diagnosis—A simple test for the localization of brain lesions, as an adjunct to the neurological examination, has been described by F H Lewy ¹ The test is performed by drawing a pin evenly across all portions of the scalp and forehead in an effort to disclose an area of hyperesthesia. This has been termed by the author as a hyperpathic area of the scalp

These hyperpathic areas have been demonstrated by Lewy in association with tumor, abscesses, subdural hematomas, arachnitis, and meningeal scar formations. This author correlated the lesion with the hyperpathic area of the scalp in 100 patients, 79 of whom had tumors. The results of these examinations showed a definite relationship between the hyperpathic scalp zone and the intracranial lesion. The exact shape of the hyperpathic area varied in different cases and its relationship to the intracranial lesion was approximate. However, the zone is

sufficiently accurate to indicate the site of operation.

Visual Field Defects—Study of the visual fields in patients with suspected tumors of the brain constitute a most valuable aid in localization. The defect of a bitemporal hemanopsia is known to be characteristic of most pituitary tumors. However, there has been much discussion as to the field defects associated with temporal and occipital lobe tumors. In a comparative study of visual field defects from patients having either temporal or occipital lobe tumors, H. S. Sanford and H. L. Bair² have made the following interesting observations: Homonymous hemanopia is the commonest visual field defect produced by tumors of the temporal and occipital lobes On the other hand, quadrantic anopias are produced much more frequently by tumors of the temporal lobe than by tumors of the occipital lobe. Normal fields are obtained with approximately the same frequency in cases of tumor of the temporal lobe and in cases of tumor of the occipital Sparing of the macula (central vision) occurs in association with both groups of tumors according to these authors, but is much commoner and of greater degree with tumors of the occipital lobe. In the cases in which necropsy specimens were available, there was no instance of sparing of the macula associated with a tumor of the temporal lobe

Visual hallucinations have been regarded as diagnostic aids in the differentiation of tumors in the temporal and occipital lobes. It has been generally accepted that temporal lobe tumors cause formed hallucinations—whereas occipital lobe tumors cause unformed hallucinations—flashes of light, colored or uncolored. The results of these investigations disprove this conception, in that both types of hallucinations occurred in either the temporal or occipital lobes

Etiology and Genesis—Trauma— The consensus has been that trauma bears little if any relationship to brain tumor formation. Recently Cox³ made a study of 150 consecutive cases of proven intracranial tumor to see what part trauma played in the clinical course He found that trauma appeared to have been related to the onset of symptoms in 4 (2.6 per cent), or possibly 5 (3.3 per cent). In 2 of these, intracranial tumors were almost certainly present at the time of injury. In 1 the microscopic study strongly suggested that the injury caused focal changes within the tumor. In 2 cases, tumors were found in the known sites of injury of a fairly severe grade It appeared as though the tumor followed the injury in 1 of these, for, although a long period elapsed between its clinical onset and the injury, it was of a slowly growing type

Genesis—In answer to the question, whether there is a genetic basis for tumors of the brain, Pass⁴ studied 30 families of patients with brain tumor. The investigation included only parents, siblings, and children; a total of 222 persons in 3 generations. Of this group, 76 had died and 109 of the living (76 per cent) were studied

In only 1 family was there a familial incidence of brain tumor. One patient with glioma in the frontal lobe had a half sister with a similar tumor. Twenty-six of the 222 relatives of patients with verified tumor of the brain, had tumors in other parts of the body, 12 of which were being and 14 malignant. Recklinghausen's disease was found in another member of the family in 3 instances.

Pass concludes that there is no evidence for a genetic basis of tumors of the brain, that there is a relation between tumor of the brain and Recklinghausen's disease, that there are grounds for the existence of an anlage to tumor forma-

tion in general and that there is no demonstrable connection between the incidence of tumor of the brain and that of other nervous and mental diseases.

Differential Diagnosis—Tumor Versus Vascular Accident—The differential diagnosis between brain tumor and vascular changes due either to arteriosclerosis or syphilis in patients past 40 years may be extremely difficult. This fact has been discussed in a paper by Hastings ⁵ The author reviewed a series of 25 cases in which the diagnosis of tumor was not entertained clinically but autopsy revealed a tumor of the brain.

In these cases, the 3 cardinal symptoms of brain tumor, headache, vomiting, and choked disc, on which the resident physician and general practitioner depend largely for a diagnosis, were absent. The following table emphasizes this point:

	N	o. Cases		
]	Present		
		Absent		
Headache		25	9	16
Vomiting		25	6	19
Choked Disc		. 14	0	*14

Thus the stress placed on cardinal symptoms may result in confusion. The average age of these patients was 56 years. Hypertension was present in only 1 patient; the remaining patients had a normal blood pressure. Two patients had a positive spinal Wassermann. The clinical diagnoses in the cases were.

Cerebral Vascular Accide Syphilis of the Brain Traumatic Arachnoiditis	nt					
Lead Encephalopathy		2 cases				
The pathological diagnoses were						
Glioma (all forms)		14 cases				
Meningeal Endothelioma		7 cases				
Metastatic Tumor .		3 cases				
Chordoma .		1 case				

Hastings divided the histories of these cases into 3 groups The first group con-

^{*} No record of 11 cases Three cases showed hyperemic discs, but no actual choking

sists of patients in whom the diagnosis was clinically possible.

In the second group, localizing signs appeared in most of the patients and there was a history not entirely compatible with a vascular lesion. The 2 cases with a positive Wassermann and the 3 which were diagnosed by laboratory findings as lead encephalopathy, fall into this intermediate group.

In the third group, the patients had a slowly progressing symptom picture with localizing signs which were, without exception, diagnosed as cerebral thrombosis.

The all important fact gained from this study, as pointed out by the author, is that a progressive history in a patient 40 or above, without the cardinal signs of increased intracranial pressure, should be considered a brain tumor until proven otherwise

Apoplectiform Onset—The importance of considering the diagnosis of brain tumor in patients who have an acute onset of hemiplegia has been reemphasized by A Stender ⁶ He reports 12 cases of verified tumor in which the first indication of a cerebral neoplasm was a sudden hemiplegia. There were no significant prodromal symptoms, at least to interfere with the usual activities of these patients.

The types of tumors in these 12 cases were Ghoblastoma-multiforme, 5, hemangioma, 2, astrocytoma or spongioblastoma polara, 3, metastatic tumor, 1; and meningioma of the frontal lobe, 1. Of these tumors 7 were in the frontal lobe, 2 in the temporal lobe, and 1 each in the basal gangha, corpus callosum, and entire hemisphere

The prodromal symptoms were head-ache in 6 and mental changes in 2 Examination of the optic discs of these patients revealed 5 without choked discs (papilledema), 2 with blurred discs, 2

with definite papilledema and 4 with marked choking. The neurological findings were not unlike those of other causes for hemiplegia. Some patients showed sensory changes, a few, hemanopic visual defects, and a few had an aphasia.

The cause for the sudden onset of hemiplegia was easily explained in 2 patients where there was a hemorrhage in and around the tumor. In the remaining 10 patients, the cause was not so apparent. A few showed extensive necrotic areas and small hemorrhages, insufficient to explain the hemiplegia. In no case could the sudden hemiplegia be attributed to an occlusion of the large blood vessel by direct pressure of the tumor suggested that reflex spasms of neighboring blood vessels may take place when a smaller branch is compressed by an expanding tumor. Marked cerebral edema occurred in all 11 cases in which autopsy was performed.

Stender believes that the sudden appearance of cerebral edema around the tumor is the most probable explanation of the apoplectiform onset in cases of tumor of the brain

Syndromes Simulating Brain Tumor—In contrast to the above are conditions which simulate brain tumor closely and are often mistaken for tumor of the brain. This fact has been recently reviewed by G. Schaltenbrand ⁷

Optic neuritis may be associated with headache and may simulate a tumor of the brain. The severe impairment of vision is an important differential point. Occasional diffuse infection of the nervous system is seen in such cases. The author refers to such cases of optic neuritis which are associated with marked cerebral and cerebellar signs. In 1 patient, extensive areas of demyelinization with intense foci of inflammatory reaction in the cerebellum, pons, and optic tracts

were found. In another patient, the brain showed a diffuse encephalomyelitis.

Turmschadel, Buerger's disease with cerebral involvement, slow thrombosis associated with arteriosclerosis, the Lawrence-Biedl-Moon syndrome, hypertension, and the Stewart-Morel syndrome may all be mistaken for tumor of the brain. Subdural hematoma, syphilis of the cerebrum, aqueductal stenosis, and traumatic arachnitis are also mentioned by the author.

It is to be noted that these syndromes or diseases make the physician consider the diagnosis of brain tumor. This is fortunate since there is something to offer in the way of treatment, whereas in the diseases mentioned, there is very little to be offered in the way of therapy for most of them.

Meningiomas

G. Horrax,⁸ in a review of 60 cases, has presented the general characteristics of these tumors. The history usually extends over a period of 1 year or longer. Therefore, these tumors grow slowly. The bone over the tumor usually shows certain characteristic changes. These tumors have a predilection for certain areas. Most of the tumors develop in the anterior half of the brain.

Horrax found that 24 of his cases were located over the cerebral convexities. These tumors were, in most instances, closely associated with the longitudinal smus. From a technical standpoint, they are the easiest to remove and are the most favorable in that the operative mortality is low.

The tuberculum scllae is another common site for these tumors. The growth is usually small because the tumor compresses the optic nerves early in its stage of development. The syndrome, as pointed out by Horrax and also by Henderson, is bilateral primary optic atrophy in a middle-aged person with progressive

loss of vision and bitemporal field defects. The sella turcica is normal when examined by the x-rays. Horrax feels that these tumors are easily handled from a surgical standpoint; however, Henderson suggests a bilateral approach. It would seem to the Reviewer that a bilateral approach in this tumor is unnecessary.

The olfactory groove is another common site for these tumors. Henderson divides them into 2 groups. The first group constitutes those tumors which develop the anterior portion of the groove and the second group, those which develop in the posterior portion of the olfactory grove Both writers comment on the fact that these tumors are invariably the largest with which the surgeon has to deal The clinical syndrome is that of anosmia which is first unilateral and since the tumor rapidly becomes bilateral, both olfactory nerves are involved In the anterior group of tumors, papilledema is the rule whereas optic atrophy with late development of papilledema is characteristic of the posterior situated tumors. Mental changes are common. In most instances it is necessary to do a 2-stage operation in order to remove the tumor.

The preolfactory area, in front of the cribriform plate, has been shown to be the origin for these tumors in 2 instances. The signs in these patients are those of increased intracranial pressure with mental sluggishness.

The sphenoid ridge is another location for these tumors. They may arise in the region of the lesser or greater wing of the sphenoid ridge. Horrax classifies these tumors as orbitotemporal since in his group of cases practically all were associated with bony involvement of the orbit. The writer feels that this adds only confusion, since in a high percentage the bony involvement described by Horrax is associated with the tumor.

Tumors arising from the lesser wing of the sphenoid ridge present the clinical syndrome of unilateral visual loss which may become bilateral, ocular palsies involving chiefly the third cranial nerve, at times loss of the sense of smell and involvement of the fifth cranial nerve Increase in intracranial pressure is a late finding.

Tumors arising from the greater wing of the sphenoid ridge do not present a definite clinical syndrome By reason of their location, they grow to enormous size before they are recognized.

The treatment as suggested by Henderson is preliminary decompression, bilateral exploration, and, if necessary, resection of the frontal lobe. This method of approach is obviously for the large tumors. In most instances, a unlateral approach is sufficient for removing the tumor. Horrax stresses the fact that when bony involvement is present, efforts should be made to remove all the infiltrated bone.

The falx and longitudinal sinus Tumors arising in this location, in most instances, grow bilaterally However. when in association with the falx only a small portion of the tumor may be opposite to the growth. These tumors produce symptoms according to their location Where the tumor is approximately equal on the 2 sides, bilateral symptoms and signs occur Their complete removal necessitates removing the sagittal smus, and Horrax states that he has removed 5 to 12 centimeters of the sinus anterior to the rolandic area. In 2 of his patients, there resulted sufficient weakness of 1 or the other leg to incapacitate them In the remaining patients, no residual signs occurred.

Gliomas of the Pons

B. J. Alpers and J. C Yaskin¹⁰ report a series of 11 cases. The typical clinical

picture in a child up to 11 or 12 years of age is as follows: The onset is often accompanied by diplopia and headache, followed in a relatively short time by paralysis of the cranial nerves (facial, trigeminal, and vagus), and by symptoms referable to the cerebellar pathways and to the pyramidal tract. All these develop more or less rapidly during an average course of about 3 months.

Examination of these patients reveals paralyses of the cranial nerves, with involvement usually of the abducens, facial, and trigeminal and sometimes of the auditory, vagus, hypoglossal, and oculomotor nerves. The paralyses are usually unilateral but may be bilateral. There are almost always some evidence of involvement of the pyramidal tracts (hemiparesis, quadriplegia, or even monoplegia), and variable cerebellar signs. Sensory disturbances are strikingly absent in practically every case. Signs of increased intracranial pressure are usually absent; choked disc is present in only a small number of cases, and the spinal fluid pressure may be normal

These authors state that a glioma confined to the dorsal part of the pons offers a particularly difficult problem in diagnosis. The difficulty in such a case is caused by the fact that the signs are limited almost entirely to paralyses of the cranial nerves, which may not be numerous. They comment upon the sign of spasm of the masseter muscle on the side of the tumor described by Rasdolsky. This difficulty leads to characteristic difficulty in opening the mouth, causing disturbance in feeding and talking.

Diplopia is considered by the authors as 1 of the most important signs since it occurs as the initial symptom. They point out that this occurs in other cases of brain tumor but it occurs late and is caused by increased intracranial pres-

sure. Pontine gliomas cause this sign to appear at the onset because of nuclear or intramedullary nerve involvement

As a point in differential diagnosis from encephalitis, the authors state that encephalitis rarely causes pyramidal and cerebellar signs. In disseminated encephalomyelitis, the long tracts are more likely to be involved than in other forms of inflammatory disease involving the base of the brain. The course of this disease should differentiate it easily from a pontile glioma.

Sometimes the differentiation of a pontile glioma from a tumor of the cerebellopontile angle is difficult. For the diagnosis of pontile glioma is the incomplete loss of hearing, atypical barany responses, and the absence of choked discs. For tumors of the cerebellopontile angle, there is the history centered about the loss of hearing, characteristic barany response, and choked discs. The authors feel that a careful attention to details will prevent unnecessary operations in patients with pontile glioma.

SPINAL CORD TUMORS

By Robert A. Groff, M.D.

Neurological Aspects—Spurling and Bradford¹³ have reviewed the symptomatology referable to herniation of the nucleus pulposus between the fourth and fifth and fifth lumbar and first sacral vertebrae The symptomatology consists of persistent sciatic pain which is often exaggerated by coughing, sneezing, or straining Associated with this pain is an incapacitating pain low in the back This latter pain precedes the sciatic pain by weeks, months, or years The back pain is usually intensified by bending or lifting Paresthesias are of extreme importance, being of far more localizing value than is the distribution of pain Tingling, prickling, cold or numb sensation occurring below the knee in the lateral aspect of the leg or in the foot are characteristic of herniated nucleus pulposus at the fourth or fifth lumbar interspace.

The signs consist of a stiff lumbar spine, a positive Lasègue sign, and diminution or absence of the ankle jerk Pressure over the fourth and fifth lumbar vertebra, their spinous processes or laterally, ofttimes elicits pain in the distribution of the sciatic nerve. Tests of the

motor power are usually not of much aid. The sensory changes are most important in making the diagnosis. Whether the hermation is at the fourth lumbar or the lumbosacral disc, the lateral aspect of the leg will be hypesthetic in most cases. However, herniation at the fourth lumbar disc usually results in hypesthesia of the anterolateral aspect of the leg with inclusion of the great toe, while hermation at the lumbosacral disc gives hypesthesia of posterolateral aspect of leg with inclusion of lateral aspect of foot

These authors feel that a diagnosis of protrusion of the nucleus pulposus can be made without the use of contrast media injected into the spinal canal. They also point out that the ligamentum posterior can be injured without producing a hermation of the nucleus.

Myelography—Chamberlain¹⁴ has reintroduced the use of air or oxygen as a means of visualizing herniations of the nucleus pulposus as well as other spinal cord lesions. His experience consists of over 300 spinograms. He considers the method reliable because in every case in which operation was performed, the level of the lesion predicted after myelographic examination, was verified by laminectomy. Air studies have not been misleading as there were no instances in which the myelograms indicated a lesion without verification at operation.

Camp,¹⁵ on the other hand, advises the use of radiopaque oil (lipiodol). His objection to the use of air or oxygen is that it is difficult to control its position and distribution. Its use is, therefore, restricted to the lumbar canal. He feels that the accuracy of the diagnosis with air is not equal to that obtained with iodized oil. He advises extreme caution in the interpretation of the x-ray films when a gas is used

In a series of 203 cases, Camp found that the results of x-ray examination

were accurate in 92.3 per cent. He found the greatest error to be at the caudal sac at the lumbosacral junction and points out that there may be a very large protrusion of the nucleus pulposus in this region without giving definite roentgen ray evidence.

Treatment—Love¹⁶ advises that as small a *laminectomy* be performed as is possible to adequately remove the nucleus. In 1 case he has performed what he has termed a partial laminectomy in which the laminae above and below on the 1 side were removed without destroying articular facets. He makes particular note of the fact that in most instances a hypertrophy of the ligamentum flavum is associated with the herniated nucleus.

CHOREA

By IRVING J. WOLMAN, M D.

Etiology—Coburn and Moore²⁴ have shown that one-half of their cases had never shown any evidences of rheumatic fever; they suggested that the physiologic background prerequisite to the development of chorea may be prepared by a number of abnormal conditions, among which the rheumatic state is the most favorable

Usher²⁵ studied 2 groups of children affected by chorea One group was made up of children who gave a history of 1 or more attacks of uncomplicated chorea—so-called "pure chorea." The other group gave a history of chorea but also had had other rheumatic manifestations in the past, such as repeated upper respiratory infections and infected tonsils, joint pains, nodules, or heart disease—"mixed chorea." Definite heart involvement as evidenced by valvular murmurs and cardiac enlargement in roentgen studies, was present in but 27

per cent of the pure choreas. In the cases with infected tonsils and recurrent upper respiratory infections, only 14 per cent were associated with endocarditis By contrast, in the group of mixed choreas, 65 per cent showed heart disease The author pointed out that a number of his cases dated from sudden psychic traumas; that the children were usually thin, active, nervous and emotional ("chorea temperament"); and that in the pure cases there was nothing to suggest that chorea is an infection from the standpoints of clinical course, temperature, pulse, blood count, or sedimentation time When chorea was associated with other evidences of rheumatic fever, a history of antecedent polyarthritis or chronic tonsillitis could usually be elicited

The contrary point of view is championed by Sutton and Dodge ²⁶ Out of 467 children having chorea at Bellevue Hospital, New York City, 133 had had

muscle and joint pains, and 243 had had frank rheumatic attacks at one time or another; only 91, or 20 per cent, showed "pure" chorea. These authors feel strongly that their statistical evidence demonstrates that chorea is a major manifestation of rheumatic fever.

Pathology — Babonneix and Lhermitte²⁷ have described the histologic lesions in the brain of a case dying of malignant Sydenham's chorea. The lesions consisted of chromatolysis and injury of the cells in the rolandic fissure and optic thalamus, with increase in the microglia and dilatation and endothelial proliferation in the neighboring blood vessels. These changes bore no resemblance to the findings in lethargic encephalitis.

McCulloch²⁸ maintains that the cerebral lesions in the few described autopsies were similar in character to those of rheumatic fever elsewhere in the body. The diseases must be considered as an exudative manifestation, rather than as a proliferative one, inasmuch as no permanent damage to brain tissue takes place. He suggests the term "encephalitis rheumatica," in order to emphasize the relationship to rheumatic fever and to describe the process in the brain

Differential Diagnosis—The clinical differentiation between chorea and athetosis has again been emphasized by Shafar ²⁹ Choreic movements are irregular, jerky, and unsustained; the successive twitchings are atypical, distinct, and separate, no matter how rapid their rate. Athetosis on the other hand consists of slow sinuous rhythmical movements blending into each other, disorganization of reciprocal innervation has taken place, and opposing muscular groups contract simultaneously. Chorea is accompanied by hypotonia which may be of very severe degree, whereas during

athetoid movements muscle tonus is raised.

Treatment — Schlesinger³⁰ presents the current views on treatment. Choreic children must be **kept in bed** and given calm and soothing nursing care. The sides of the cot may be padded if movements are violent.

Sedatives are helpful. He suggests choral hydrate, 1 grain (0.065 Gm.) for every year of age, 3 or 4 times each 24 hours, with 10 grains (0.65 Gm.) as the top individual dose; chloretone can be given, in somewhat smaller quantities. with 8 grains (0.52 Gm.) as the maximum single dose. In this country phenobarbital, $\frac{1}{4}$ to $\frac{1}{2}$ grain (16 to 30) mg) thrice daily is the most commonly used sedative. Schlesinger uses salicylates, such as aspirin or pyramidon, especially the latter, in doses of 5 to 10 grains (0.32 to 0.65 Gm) 3 times a day, depending on the patients' age. With all these drugs, regular evacuation of the bowels is most important. Nirvanol (phenyl-ethyl-hydantoin), $1\frac{1}{2}$ to $2\frac{1}{4}$ grains (01 to 015 Gm) twice daily for a week or 10 days, until the rash appears, is recommended, although most American clinics have now abandoned its use. For high temperature therapy, the Kettering hypertherm apparatus is better than typhoid vaccine intravenously

During convalescence, the patient should receive a regular diet, with massage and occupational therapy. If a residue of chorea persists, children are often benefited by a mixture containing liquor arsenicalis, 2 to 3 minims (0.13 to 0.19 cc.), potassium bromide, 6 grains (0.39 Gm.), compound tincture of cardamom, 10 minims (0.6 cc.), in a dessertspoonful of water thrice daily. The presence of heart complications necessitates special therapy directed to that condition.

CRANIOCEREBRAL TRAUMA

By RICHARD L. MASLAND, M.D.

Pathology — During the past year there has been a marked tendency to turn away from the theory of cerebral edema and increased intracranial pressure, and to search for other causes of death in cases of severe head injury. This point of view is best summarized by Browder and Meyers¹⁷ as follows:

The theory of Kocher describes 4 stages through which the patient passes with progressive increase in intracranial pressure

- (a) Stage of accommodation This is characterized by headache, apathy and slight increase in intracranial pressure.
- (b) Stage of early manifest symptoms The intracranial pressure is now increased so as to expel blood from the capillaries, and cause cerebral anemia. The symptoms are rising blood pressure, slowing of the pulse due to vagal stimulation, facial cyanosis, headache, restlessness and slow respiration.
- (c) Stage of advanced manifest symptoms At this point, medullary anemia becomes marked. The blood pressure is high and variable, pulse 40 to 50, respiration often Cheyne-Stokes, and there is marked facial cyanosis.
- (d) Stage of medullary collapse When intracranial pressure becomes too high, there is irreparable damage to the medulla. Blood pressure falls, the pulse becomes rapid and thready, and the patient goes into a shocklike state and dies

On the basis of this theory, treatment with dehydration and decompressive operations was instituted, but the clinical results have been disappointing. In the first place, the classical pattern of signs, consisting of a steady rise above normal levels of systemic blood pressure, concomitant fall in pulse rate, decrease in respiratory rate, stupor, vomiting, etc., which has been alleged to indicate that the intracranial pressure is on the increase, has not been observed in a large series of cases with brain insults. Furthermore, it has been impossible clin-

ically, to find any correlation between the patient's condition and his spinal fluid pressure. This correlation also breaks down experimentally. In patients with large skull defects, the intracranial pressure may be raised by applying pressure over the defect. In these cases, it is necessary to raise the pressure to well over diastolic blood pressure before any symptoms develop. Similarly, the intraventricular pressure may be raised experimentally in patients subjected to ventricular tap, by injection of saline into the ventricles. Here again, in order to produce symptoms, the pressure must be raised well above that ever found clinically in head injury cases. Finally, it has been necessary to reevaluate the effect of intravenous hypertonic solutions Although hypertonic glucose, sucrose, and sorbital are found to reduce the cerebrospinal fluid pressure of normal animals, their action on the miured brain is often the reverse, and is always unpredictable In a few cases, the administration of hypertonic glucose has been followed by sudden death

On the basis of these observations, Browder and Meyers conclude that the changes in the constitutional, neurologic, and psychologic states of patients showing evidence of severe trauma of the brain are not explainable in terms of increased intracramal tension per se

The difficulty in attempting to explain all cases of head training on the basis of increased intracramal pressure is further emphasized by Delannoy and Demarez. who describe a syndrome of hypotension of the cerebrospinal fluid. They have observed this condition in from 10 to 20 per cent of head injury cases. The reduction in pressure may occur either with severe or mild injury which does not

involve skull fracture, and thus is not due to leak of the spinal fluid. It may be observed in the early stages of acute injury, as a secondary manifestation, or even as a sequel lasting months or years after the accident In the acute form, the reduction of pressure is thought to be the result of shock, with failure of general circulation and concentration of the blood, both of which serve to impair the production of cerebrospinal fluid. Spinal puncture and removal of cerebrospinal fluid at this stage may be disastrous, as it serves only to increase cerebral hemorrhage and edema On the other hand, the administration of large amounts of normal saline may be a valuable aid. In the secondary and chronic forms of cerebrospinal hypotension, the fundamental pathology is thought to lie in the choroid plexus. It is suggested that filtration is impaired either by injury to the plexus, or by disturbance of its vasomotor control Treatment in these cases is directed toward stimulation of the plexus by cerebral vasodilator drugs.

It is thus becoming apparent that clinical evidence does not support the belief that cerebral edema and compression are responsible for the symptoms in all head injury cases. This problem has received further consideration in the laboratory Shapiro and Jackson¹⁹ analyzed the brains of "normal" individuals, patients dving from head injury, and patients with alcoholic or cardiac "wet brains," in an effort to determine the location of fluid in each case. Their results may be summarized as follows.

- 1 The total weight of the posttraumatic brain is 30 to 50 Gm greater than normal
- 2 The ventricles of the posttraumatic brain are often distended and filled with fluid, but the subarachnoid spaces are dry, as though compressed and obstructed
- 3. By dehydration with sulfuric acid, the water content of the posttraumatic brain was found to be lower than the normal brain, and much lower than the alcoholic brain.

4. Analysis of the iron contents shows that the increased weight of the posttraumatic brain may be attributed to the presence of an increased amount of blood. This may possibly be due to vascular dilatation, but it is suggested that it is probably due to multiple punctate hemorrhages within the brain.

On the basis of these studies, the authors conclude that following head injury the patient is suffering primarily from uncontrolled internal hemorrhage within the cranial cavity. In order to compensate for the increased brain volume which results from blood in the tissues, there is a reduction in subarachnoid and extracellular fluids. The posttraumatic brain is not edematous, but dehydrated.

As a result of this type of evidence, opinion has become much more conservative as to the use of decompressive and dehydrating measures in treatment. An excellent review of treatment is provided by Crawford²⁰ and by Browder and Meyers ¹⁷

Following the emergency treatment of shock, if present, and when an operable lesion has been ruled out, the only remaining treatment is supportive. Suggested therapy is as follows:

- 1 **Posture**—Bed position must be such as to permit free venous drainage from the brain, and free respiratory exchange. The semi-Fowler position may assist the former, but it is important to keep the airway clear.
- 2 Sufficient **sedation** to insure against excessive motor activity. Moderate doses of **chloral hydrate**, **paraldehyde** or the **barbiturates** are recommended if necessary.
- 3 Control of temperature **Cooling rubs** or **enemas** should be given if the temperature exceeds 102° F (39° C) Measures are much more effective if instituted at this level than with higher temperatures
- 4 Control of fluid balance, Browder and Myers suggest the use of a nasal tube, and the administration of 6% ounces (2000 cc) of fluid in each 24-hour period **Magnesium sulfate**, 3 drams, may be given if dehydration is desired
- 5 Cellular metabolism Crawford emphasizes the importance of maintaining adequate nutrition of the damaged cells, and believes

that anoxia is responsible for much irreparable cerebral injury. This anoxia is often due to interference with circulation, but it may be increased by injudicious use of drugs which may further impair the circulation and also reduce cellular metabolism by a direct toxic effect. For this reason, he refrains from the use of sedatives, particularly morphine and the barbiturates, which are known to reduce cellular oxygen metabolism. The blood sugar level is kept elevated by intravenous administration of glucose when needed. In unconscious patients, the blood oxygen saturation is kept above 90 per cent by the use of the *Hartman oxygen apparatus*.

- 6 Lumbar Puncture—This procedure may be necessary to determine the intraspinal pressure, and to indicate the presence and amount of bleeding, but it should be deferred until the stage of acute hemorrhage is past Repeated lumbar puncture is valuable in removing blood from subarachnoid spaces, but should be used only for grossly bloody fluids.
- 7 **Dehydration**—Hypertonic solutions are used only in cases in which edema develops as a complicating factor. These cases are relatively rare

The other indications for surgery, compound fracture and depressed fracture, are quite generally accepted Glaser and Shafer, 21 however, made a follow-up study of 91 cases of depressed skull fracture They found that the sequelae of this type of injury were not due to the depression of the bone, but were due to the injury of the brain which occurred at the time when the bone was depressed Operation did not appear to have reduced the incidence of these sequelae They conclude that elevation should be confined to fractures of a fragmented or spiculated nature, wherein the dura has been perforated and the brain traumatized, or when the depression is over functioning cortical areas

The Posttraumatic Syndrome

With the increasing factor of compensation, the diagnosis and treatment of posttraumatic cases is assuming great importance. Chief among the problems which these cases present is the determination of the degree of disability, and evaluation of the relative importance of the organic and functional elements.

The routine study of posttraumatic cases, as suggested by Munro,22 emphasizes the importance of searching for evidence of organic disease. The probable severity of the injury is first determined from the history. The age of the patient, duration of unconsciousness, and findings by x-rays and lumbar puncture at the time of the accident provide considerable information in regard to the probable extent of brain damage. A complete physical examination and laboratory studies including head x-rays, barany. and lumbar puncture are necessary in all cases. In a large proportion of cases, presenting the usual subjective symptoms (headache, dizziness), these studies will be entirely negative, and one is faced with the problem of differentiating the patient who is malingering or neurotic from the patient who has brain atrophy or subdural hematoma

Munro does not believe that this distinction can be made clinically, and suggests 2 further diagnostic procedures which should be carried out on those patients willing to undertake the risk involved. The first of these is encephalography, which, in his experience, has demonstrated cortical atrophy with a high degree of accuracy, and solid hematomas sufficiently often to be a valuable adjunct in their diagnosis cause of the fact that encephalography regularly fails to demonstrate liquid hematomas, it is suggested that exploratory trephine should be employed in all questionable cases It is pointed out that subdural hematoma developed in 17 per cent of all cases of craniocerebral injury hospitalized at the time of the accident. The frequency of this condition, and the fact that the liquid form is particularly

common in the chronic "posttraumatic" case, makes the exploratory trephine a justifiable procedure. In the author's experience of over 300 trephines only 2 per cent of these have been negative, and many patients who might otherwise have been classed as posttraumatic neurosis have been permanently cured.

All writers on this subject emphasize the importance of making a careful study of the patient's previous character and past history in order to evaluate his reaction to the illness. Schaller²³ defines the posttraumatic psychoneurosis as the result of a combination of character defect, wishful thinking, and time to meditate, and offers the following differential diagnosis:

Posttraumatic Posttraumatic Psychoneurosis Encephalopathy 1 Does not wish to Wishes to work. work.

2 Depressed, emo- Euphoric, aggressive, tional, complainirritable ing.

3 Mentally alert Amnesia of injury, memory and concentraction difficult

Posttraumatic Psychoneurosis

herent personality defects

Posttraumatic Encephalopathy

4 Aggravation of in- Changes from original personality.

5 Injury frequently Injury often severe with long unconslight sciousness.

toms and signs.

6. Hysterical symp- No hysterical symptoms and signs

7 Exaggeration and None elaboration in statement and behavior.

8 Course Tendency Course. Tendency to to aggravation improvement.

termination of compensation or settlement

9 Favorable effect of No effect of termination of compensation or settlement

10 Multiplicity, Constant and precise changeability symptomatology and indefiniteness of symptoms

11 Headache rarely Headache frequently absent. absent

12 Dizziness Giddi- Dizziness Vertigo ness

13 No disturbance of Intolerance to heat tolerance to heat and alcohol or alcohol

ELECTROENCEPHALOGRAPHY

By Joseph Hughes, M.D.

The electroencephalograph is a clinical instrument used to record brain potentials. The best type of instrument consists of either 2 or 3 channels of aniphification which in turn drive either ink-writing or cathode ray oscillographs. Electrodes placed on the patients' scalp feed these amplifiers. The records obtained are known as an electroencephalogram or E. E. G. They represent for the most part electrical activity in the underlying cerebral cortex Muscle potentials will also record and in unco-operative patients will confuse the record.

Localization of Cerebral Lesions by the E. E. G.—In 1935 Kornmueller, 31 Foerster and Altenburger 32 confirmed Berger's observation on tumors and reported their findings of slow potentials from the area surrounding tu-In 1936 to 1937, Walter^{33, 34} succeeded in localizing tumors in 12 patients and his negative electrical findings on 26 brain tumor suspects were upheld by their subsequent clinical course Walter introduced the use of paired electrodes for localizing purposes. In this manner he was able to lead from 2 areas

of the scalp simultaneously. In 1939 Williams and Gibbs,35 using a similar technic, studied 105 cases of suspected intracranial lesions and succeeded in localizing the lesions by their electrical studies in each of the 50 patients of this group in whom the lesion was verified clinically. These lesions consisted of cortical tumors, obstruction of the posterior fossa, long standing cerebral trauma. abscesses, acute encephalitis, subdural hematoma, porencephalic cyst, hemorrhage, and infarction. Forty-one patients showed a normal E.E.G. with subsequent clinical examination revealing no lesions. In the 14 remaining patients of this study, it was not possible, because of lack of clinical as well as pathological data, to confirm the abnormal electrical findings Hughes has localized a group of frontal lobe tumors with similar success. His findings with posterior fossa tumors indicate that tumors in this location will not be located unless they compress the overlying cerebral hemispheres

Diagnosis of Epilepsy—Gibbs, Davis and Lennox³⁶ in 1935 reported characteristic findings in the E E G in epilepsy. To bring out these findings, a single scalp lead is used rather than paired leads. Petit mal is characterized by either a high voltage spike and slow wave which occurs at a 3 per second frequency or at a 2 per second frequency. Grand mal shows a burst of increasing fast high voltage waves. Psychic equivalents show high voltage square and 6 per second waves.

Jasper and Hawke,³⁷ in 1938, localized the origin of epileptic seizure waves by "triangulation." This, however, has been largely replaced by the method of phase reversal used by Walter 8

In epilepsy, the degree of abnormal electrical activity shown in the E. E. G. varies as the clinical condition of the patient so that it may be at a minimal or subclinical level between attacks or it may be absent from any single examination. Repeated examinations may be required before seizure waves are observed. The petit mal type of wave may be brought out by overbreathing or lowering the blood sugar with insulin.³⁸

Diagnosis of Behavior Problems of Children—An important contribution to this problem has been made by the electroencephalographic study of 71 behavior problem children by Jasper, Solomon and Bradley.³⁹ Over half of this group were shown to have distinctly abnormal electroencephalograms Out of 30 of these children who were classified clinically as being hyperactive, variable and irritable in their behavior, 21 showed brain waves of the epileptic type. Of 11 children who were classified as schizoid, 7 showed abnormal waves, and of 32 whose behavior was inconstant and variable, only 19 showed normal waves

Rôle of the E.E.G. in Clinical Practice—The usefulness of an E. E. G. as another aid in diagnosis can be accepted as having been established. Particularly is this true in cases of convulsive seizure or in instances of suspected cortical lesions. It is a simple procedure which results in no discomfort for the patient and as such it may be readily recommended to patients when clinically it does not seem justifiable to do an encephalogram In skilled hands, it will prove a valuable adjunct, but as there are many artefacts which can appear in the examination that could be confused with cortical lesions, its use should be restricted to those familiar with such errors

ENCEPHALITIS

By Henry A Davidson, M.S., M.D.

Pathogenesis-Increasing interest in the possibility that the horse may be the carrier of one type of human encephalitis is reflected in the 1939 literature. Two editorials, 1 in the Journal of the American Medical Association,40 and 1 in the British Medical Journal,41 underscore this possibility. Fothergill, Holden and Wyckoff⁴² describe a fatal case of equine encephalomyelitis in a laboratory worker Their patient had been working with the virus, and was apparently infected by it She developed headache, fever, and convulsions and died on the eighth day. At autopsy the specific virus was isolated from the blood and brain Sixteen cases of equine encephalomyelitis in human beings are listed by Larimer and Wiesser 43 Their patients lived in a part of Iowa in which an epidemic of equine encephalitis was prevalent, and most of them had had contact with horses. Four of the 16 patients died. Howett44 describes an epidemic of encephalitis in California in which 40 deaths occurred. Positive neutralization to the equine virus was obtained in 37 per cent of the cases. Predominantly, the persons reactive to the equine virus were young people living in the swampy parts of the San Joaquin Valley It seems likely that direct transmission from the horse to the human must be rare, since the disease in horses is swiftly fatal, and the virus vanishes quickly from the blood of infected ani-Presumably, the virus is transmitted through some intermediate carrier, possibly mosquitoes, pigeons, geese. or ducks

Another concept of the pathogenesis of encephalitis is offered by Putnam and Alexander ⁴⁵ They suggest that the underlying change common to all forms

of encephalitis and encephalomyelitis is thrombosis of small vessels. These thrombi may originate through local areas of asphyxiation, phlebitis, suppurative foci or endarteritis.

Secondary Encephalitis — Many cases of encephalitis secondary to measles, mumps, typhoid fever, sulfamilamide administration, and neoarsphenamine were reported in 1939.

Peluffo and Castells⁴⁶ warn that the *typhoid* bacillus has a special affinity for the nervous system, especially in children They report 4 cases of typhoid encephalitis, 3 of which were fatal The encephalitic symptoms included bulbar, cerebellar, mesencephalic, and convulsive manifestations. Hope for treatment depends, they believe, on the success of immunotransfusion.

Three cases of measles encephalitis were reported, 2 by Malanud, 47 and 1 by Ziskind and Schattenberg 48. In 1 of Malanud's cases the patient was left with permanent hemiplegic manifestations. In the other, postencephalitic changes took the form of hyperkinesis, mental retardation and ataxia. In the case cited by Ziskind and Schattenberg, 48 the patient died 8 months after the attack of measles. Both observers were impressed by the predominance of white matter lesions in this form of encephalitis.

Reviewing 38 cases of mumps meningoencephalitis, Birnberg ⁴⁹ points out that clinical symptoms may appear at any time between the first and tenth day after the onset of the parotitis. Headache is the usual presenting symptom. Other features are fever, vomiting, nuchal rigidity, and a positive Kernig sign. The spinal fluid cell count and pressure are usually high, and lumbar puncture is recommended as a method of relieving the headache by lowering intracranial pressure. Duration of the encephalitis fluctuates between 3 and 11 days

Two cases of encephalitis due to sulfanilamide are reported by Fisher.⁵⁰ In 1 case, the total sulfanilamide dosage was only 3½ drams (14 Gm), in the other, 4½ drams (18 Gm.). The low level of the dosage suggests that the patients must have suffered from some unusual susceptibility

Hemorrhagic Encephalitis-A common cause of hemorrhagic encephalitis is acute arsenical intoxication, usually due to injection of arsphenamine or neoarsphenamine. Paley and Pleshette⁵¹ have collected 158 cases, and call attention to the fact that a large proportion occurred in pregnant women. Generally, these patients developed the encephalitis after the second or third dose Warning symptoms were headache, fever, vertigo, and diffuse body pains. The encephalitis was fatal in most cases, and Pleshette and Paley caution practitioners against large doses of neoarsphenamine in pregnant women Another form of hemorrhagic encephalitis is Wernicke's disease, in which paralysis of eye muscles is a feature Until recently, alcohol was considered the cause, and, indeed, most of the cases occurred in chronic alcoholics However, in common with other evidences that many apparently "alcoholic" symptoms are of avitaminotic origin, modern investigators stress the vitamindeficiency aspect of the disorder. Thus Ecker and Woltman⁵² report a case of Wernicke's disease in which the patient suffered a marked loss of gastric secretions and a corresponding deficiency in assimilation And Campbell and Biggart⁵³ review 12 cases of Wernicke's encephalopathy in only 1 of which alcohol could be established as a cause. Both groups of authors agree that high dosages

of vitamins B_1 and C (especially the former) would seem to be rational therapy. The disease is diagnosed by vertigo, somnolence, reeling gait, and weakness in the eye muscles.

Otogenic Encephalitis—Atkinson⁵⁴ states that otogenic infection may sometimes produce a localized nonsuppurative encephalitis which clinically resembles brain abscess Reviewing 25 cases, 15 of his own, Atkinson finds the temporal lobe the commonest locus of the lesion. To distinguish chronic infectious encephalitis from brain abscess, he depends largely on spinal fluid findings. 55 "Hundreds of polymononuclears are found against tens of mononuclears in abscess." The "dissociation syndrome of Borries" (diminution of spinal fluid findings with aggravation of clinical signs) is more suggestive of abscess, while a joint alteration in laboratory and clinical findings speaks more suggestively of nonsuppurative infection Headache, fever, and inconstant eye-ground changes are usually found in localized encephalitis These, in turn, are to be distinguished from acute infective encephalitis in which the agitation or delirium contrasts clearly with the lethargy or stupor of the victim of brain abscess Temperature which, in brain abscess is but little elevated, is likely to be very high in acute otogenic encephalitis Spinal fluid lymphocytosis in acute cases always suggests the nonsuppurative lesion

The distinction between nonsuppurative localized encephalitis and brain abscess which it so closely resembles, is of considerable practical importance because of the difference in therapy. Exploration is inadvisable in a nonpyogenic lesion, and excision is especially dangerous since surgical manipulation of such an area may cause infection to spread. *Local decompression*, however, may be indicated to relieve the intracranial hyper-

tension. *Hypertonic solutions* may be injected in *acute* cases, but should be shunned in chronic encephalitis. *Lumbar puncture* is a useful therapeutic aid in nonsuppurative cases

Torular Encephalitis—The Torula histolytica (Cryptococcus meningitidis) occasionally causes meningoencephalitis. Greenfield, Martin and Moore⁵⁶ report a case in which the diagnosis was not made during life, and remind practitioners that in chronic infectious lesions within the skull, the spinal fluid should always be examined for parasites.

Pseudotumoral Encephalitis — Localized encephalitis may mimic brain tumor in its symptomatology. Both may show evidence of intracranial hypertension including choked disc. Roger, Arnaud and Paillas⁵⁷ find that the most reliable differentiating sign is absence of retinal vessel hypertension in encephalitis, its presence in tumor. In doubtful cases, ventriculography is indicated as being both therapeutically helpful and diagnostically significant

Prognosis—Gardere, Dauvergne and Bertrand⁵⁸ find that the more serious forms of encephalitis in children are those secondary to the exanthemata, especially pertussis and measles. Convulsions and somnolence are especially critical signs in children with encephalitis Evidences of bulbar involvement are also frequent omens of a fatal outcome. The general mortality rate in a series studied by Breslich, Rowe and Lehman⁵⁹ was 22 per cent. In this group, 25 per cent of the adults but none of the children died.

Treatment—Little was added to our treatment technic for acute encephalitis during 1939. Larimer and Wiesser⁴³ describe a therapeutic program, essential features of which are: Repeated spinal punctures; fluid intravenously; morphine for relief of headache; magnesium sulfate by mouth and rectum When the cause is certain, convalescent serum may be used Sulfanilamide was not effective, but further trials of this drug would seem worth while.

ENCEPHALOMYELITIS

By Eli Marcovitz, M D

Pathology—T J Putnam and L Alexander 60 discuss the "encephalomyelitic reaction" and its probable pathogenesis. This inflammatory reaction has been accepted by many authors as evidence of an infectious process. It occurs in many types of disease of the nervous system, but is more typical and widespread in the group of diseases known as "dissemmated encephalomyelitis" than in any other. In the early stages of this reaction, the authors hold, congestion and thrombosis of vessels may be observed with considerable regularity. Since evidences of vascular occlusion are so com-

mon in relation to the "encephalomyelitic reaction," since it is difficult to find instances of similar types of vascular occlusion without it and since it may be produced experimentally by appropriate interference with the blood supply of the brain, the authors feel that it is reasonable to conclude that the vascular occlusion is primary to the histological process.

Endarteritis, endophlebitis, asphyxia, propagation from a suppurative focus, the experimental injection of organ extracts and bacterial products and other processes have all produced thrombi and the subsequent "encephalomyelitic re-

action." The authors insist, therefore, that the histologic process of "encephalomyelitic reaction" cannot be considered as proof of the existence of an infection. Evidence for an infectious etiology of any of the types of encephalomyelitides must be sought in other directions, particularly by the fulfilling of Koch's postulates.

In 1 of a series of articles in which he attempts the histopathological differentiation of the various demyelinating diseases, George B. Hassin⁶¹ reports the studies of a case of disseminated encephalonivelitis and differentiates it from multiple sclerosis, multiple degenerative softening (acute multiple sclerosis) and postvaccinial encephalitis. In this case he found massive hematogenous infiltrations of the blood vessels of the meninges. spinal roots, spinal cord, medulla, pons, basal ganglia, internal capsule and cornu ammonis. Therefore, he calls it an inflammatory process and terms it meningoencephalomyeloradiculitis He believes that foci of degeneration in disseminated encephalomyelitis are a complication in fatal cases and not an integral part of the picture The reactive changes in such areas are mainly microglial. These do not occur in multiple sclerosis, and denote either a vascular factor or severe toxemia. He concludes that encephalomyelitis, because of the vascular hematogenous infiltrations, differs from multiple sclerosis and from multiple degenerative softening (acute multiple sclerosis)

N. Malamud⁶² reports the neuropathological findings in 2 cases who survived, 5 and 4 years respectively, attacks of postmeasles encephalitis. Both cases clinically presented permanent sequelae, in 1 case hemiplegic manifestations, in the other hyperkinesis, personality change, mental enfeeblement, and ataxia. In both cases the course was not progressive, the symptoms remaining stationary and, in 1 case, receding.

The lesions were localized exclusively in the white matter, in sites typical of the lesions in acute postmeasles encepha-They presented the histological litis. characteristics of the end results of a definite inflammatory process with dense glial scars and poorly-outlined foci of demyelination. The author points out various features which distinguish this picture from that of multiple sclerosis. He concludes that clinically and pathologically the receding inflammatory process of measles encephalomyelitis is to be distinguished from the progressive primary demyelinating disorders (such as multiple sclerosis).

R F. Teemster⁶³ reports on 38 cases of a form of human encephalitis occurring in Massachusetts and Rhode Island in an epidemic associated with an epizootic of equine encephalomyelitis. Of the 38 cases which were investigated, 25 died. Of these, 8 cases were proven to be due to the eastern virus of equine encephalomyelitis, by the isolation of the virus from the brain postmortem.

Seven more cases, in which the virus was not isolated, showed characteristic gross and microscopic lesions. Of those cases which recovered, 6 were studied to determine antibody titer. Four showed a high antibody titer, 2 were negative.

The 38 cases were evenly divided between the sexes. It appeared that children under the age of 2 years were particularly susceptible, comprising 37 per cent of the entire series; 50 per cent of the cases were under 5 years of age and 67 per cent were under 10 years.

There were no instances of multiple cases in a family and no contact infection was traced. Contact with horses was casual or absent but it was noted that mosquitoes were unusually prevalent.

Clinically, the onset was sudden, with fever, irritability or drowsiness, cyanosis, and convulsions. In the older children and adults, the onset was slower, over a period of 4 to 10 days. In 2 cases there was a remission lasting 1 day Headache and dizziness were prominent, vomiting occurred in some cases Other signs were coma or stupor, with tremors or twitchings, nuchal rigidity, tenseness of the anterior fontanelle, sluggish pupils and, in 1 case, photophobia The temperature was elevated, between 102° and 104° F (39° and 40° C), rising higher in the fatal cases and diminishing by lysis over 4 to 5 days in those which recovered The cerebrospinal fluid was under increased pressure, the average being 240 The fluid was hazy to mm of water "ground-glass" in appearance, containing 200 to 2000 cells, of which 60 to 90 per cent were polymorphonuclear leukocytes There were 95 to 185 mg of total protein

per 100 cc Sugar content was normal or slightly elevated and no organisms were isolated. There was a leukocytosis in the blood, ranging from 14,600 to 65,900 cells, with 75 to 90 per cent polynuclear cells. The figures above 35,000 were obtained in children with pertussis. If the patient lived more than 2 or 3 days, there was a gradual drop in the leukocyte count in the spinal fluid and blood with a change to mononuclear cells.

Some of the suspected cases recovered completely but it appeared that others would show paralyses, mental changes and other permanent residuals.

Histopathological studies revealed a diffuse acute meningoencephalitis, characterized by intense polynuclear and monocytic infiltration in the perivascular spaces and to a minor degree in the meninges, and by a widespread destruction of nerve cells

EPILEPSY

By Thomas K. Rathmell, M.D.

Autonomic epilepsy is characterized by a strong rapid pulse and a rise in the systolic blood pressure, frequently of 100 points Electrocardiographic studies of 54 seizures made by Erickson⁶⁴ showed no evidence of asystole, although in many of the attacks there was a simultaneous disappearance of the radial pulse and of cerebral pulsation. Increased muscle tension or movement probably explains this finding. The cardiac rate may show acceleration or no change during a seizure Temporary T wave changes apparently due to deficient oxygenation of the myocardium are occasionally seen Blood pressure changes are variable

Bellet⁶⁵ found prolongations of the QT complex of the electrocardiogram in

cases of convulsions in adults due to idiopathic hypocalcenia. The more severe the hypocalcenia, the greater the prolongation of the QT interval which may often be 50 to 60 per cent above normal

Hypersensitive carotid sinus stimulation by pressure may cause syncope or convulsions. The incidence of this syndrome is but 0.9 per cent in 1000 cases studied by Robinson, 66 while Lennox found no instance of the carotid sinus syndrome in 150 epileptics, however, it must be considered as a possible etiologic cause of epileptic convulsions. Criteria for its recognition are: The occurrence of attacks while in the upright position; aura directly precedes the attack, stimu-

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lus is pressure of sudden movement or constricting neckwear, attacks last from seconds to minutes and the sensorium clears rapidly but recurrences may be within hours, days, or years. Phenobarbital has no effect on incidence of either spontaneous or induced sinus seizures

In patients with the cerebral changes due to old age and arteriosclerosis. Tompkins⁶⁷ records convulsions in 7 per cent, episodic attacks which might be epileptoid in 6 per cent, and profound and lasting changes of consciousness in 3 per cent of 100 cases of senile and arteriosclerotic psychoses which he investigated to determine the incidence of convulsive manifestations

Hereditary epilepsy in the biological meaning of the term "hereditary" does not exist according to Wertheimer 68 He concludes that essential or idiopathic epilepsy is a sequel of obstetric intracramal lesions, especially of intracramal hemorrhages, which may have escaped observation because their symptoms were slight Studies of labor in epileptic women showed a high incidence of precipitate deliveries. Brown⁶⁹ stresses the fact that there are constitutional or inborn differences between mentally deteriorated and nondeteriorated epileptic patients as well as important clinical differences. Lowenbach⁷⁰ studied 37 persons who were relatives of 2 epileptic patients but themselves without a clinical sign of epilepsy Seventeen showed an abnormal electroencephalogram pattern while 3 showed spike and wave groups pathognomonic of petit mal. He also observed a pair of identical twins, 1 epileptic, the other normal but with similar electroencephalograms Lowenbach concluded that the abnormal features are an expression of an inherited functional instability of the central nervous system and that other unknown factors have to be present besides cerebral dysrhythmia in order to justify the clinical "epilepsy."

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Lennox and the Gibbs'⁷¹ obtained definitely abnormal electroencephalograms in 54 per cent of the relatives of epileptics as compared to but 6 per cent in a control group unrelated to epileptics. They feel that cortical rhythm is a fundamental constitutional characteristic and that the cerebral dysrhythmia associated with epilepsy is inheritable, perhaps as a dominant mendelian trait. If an epileptic marries, he should choose a mate with normal brain waves. Marriage is safer for such a pair than for 2 persons whose personal and family histories are free of seizures but who both have cortical dysrhythmia

One thousand cases of childhood convulsions were reviewed by Peterman,⁷² none of which was due to hypoglycemia or hyperinsulinism Etiological factors were

	Per Cent
Acute infection	340
Idiopathic epilepsy	23 6
Cerebral birth injury or residue	15 5
Miscellaneous causes	127
Spasmophilia or tetany	89
Not established	5.3

Syphilitic epilepsies, according to Babalian, 73 are not as rare as the majority of authors believe, and by a complete family inquiry, the hereditary syphilis may be found. Cases due to toxic infectious diseases and obstetrical injury must be eliminated before treatment with bismuth or mercury is instituted. Following the first convulsions of infancy there may be a period of deceiving calin during which seizures are absent. It is during this interval that the syphilitic epilepsies may be most favorably influenced by therapy

Fox believes that the usual estimate of 2 epileptics per 1000 of population is too low 74. This condition is 1 which merits most careful and planned therapy as

many suffer social handicaps because of their seizures or from some form of mental abnormality. The initial step in the treatment of every case should be a short period of residence in a well equipped neurological center. During this time, a clinical examination of the central nervous system may be done as well as observation of the attacks, study of the blood and cerebrospinal fluid, x-rays of the skull and encephalography. Electroencephalographic records during and between the seizures may be secured with ventriculography in selected cases A survey of the patient's general health and a check for endocrine anomalies is important Intelligence of the patient should be tested by standard methods when indicated and observations made of his behavior and response to various situations Such a procedure would enable seizures of hysterical origin to be recognized as well as permitting an early diagnosis of the disability to be considered in making plans for the future, thereby preventing the younger patients from drifting into unselected and unsuitable employment Ideal work for the epileptic must be on the level, removed from machinery or moving traffic and guarded from contact with water, fire, or electricity.73

The efficacy of dehydration in controling convulsions is questioned by workers⁷⁶ whose studies showed that although excessive amounts of water (7000 ml) were a positive factor in precipitating seizures, average amounts did not have this effect as only one-half of the epileptic patients and none of the controls had convulsions following hydration

Treatment—The anticonvulsant effect of brilliant vital red is most pronounced in petit mal seizures. Cobb and his associates 77 considered its trial justifiable in cases of intractable epilepsy. The dye is given intravenously. The safest and most satisfactory procedure in the administra-

tion of brilliant vital red which has been accompanied by the least amount of renal irritation and other transitory effects is as follows:⁷⁸ 10 to 15 ml of a 1 per cent solution of the dye are given daily for 2 or 3 days at the start of treatment After these small initial doses, the dye is omitted for a day, then 30 ml. are given 2 or 3 days in succession, followed by omission on 1 day.

Amounts varying from 115 ml to 1396 ml have been given intravenously Within a few days after the injection of the dye. the skin, sclera, and tears show a tinge of redness which deepens as the treatment progresses Within 2 months after stopping treatment, the skin color returns to normal The mechanism of the anticonvulsant action of the dye is uncertain. but Aird79 has shown that in animals with experimental epilepsy, brilliant vital red renders the endothelium of the hematoencephalic barrier impermeable to the passage of convulsive agents and suggests that an analogous situation may or may not exist in human cases which have been afforded protection from the epileptic seizure

Thyroid extract in closes of ½ grain (0.032 Gm) and 1 grain (0.065 Gm) caused improvement in the number of seizures of 35 to 40 per cent of the patients who were studied by Doohttle,80 while 60 to 65 per cent were apparently made worse by the drug. Some of the cases were also taking phenobarbital Patients with unstable diastolic pressure or with a diastolic pressure which is easily decreased by thyroid extract should not be given this drug.

Leroy⁸¹ believes, as a result of its trial in a single case, that the intravenous injection of 8 grains (0.518 Gm.) of *metrazol* has a beneficial influence on the agitated phase following the convulsive seizure of epileptics

Boron preparations, which are a constituent of some popular reducing remedies, have been used by Verjaal, 82 always in combination with phenobarbital in 100 adults who reacted inadequately to large doses of bromide and phenobarbital. Seizures were stopped in 13 cases and reduced to less than one-third in 27 when administered from 1 to 3 or 4 times daily in the following combinations:

Phenobarbital 1 0 grain (0 065 Gm) Sodium Borate 75 grains (0.484 Gm) Boric Acid . 75 grains (0 484 Gm)

Among the undesirable complications that may result from this medication are exanthemata, gastrointestinal disturbances, fever, albuminuria, alopecia areata, and emaciation. Studies on the metabolism of boron suggested that its favorable effect on epilepsy can be ascribed to its action on the biologic condition of the organism.

Treatment of clinical seizures in children has been well summarized by Peterman 72 He advises that one should never use opium derivatives in attempts to relieve the seizure but that if there is an associated high fever, cool sponges or packs and a cool hypertonic saline enema are indicated Spinal puncture should always be done when facilities per-Administration of *chloroform* by inhalation is particularly effective for status epilepticus Magnesium sulfate may be given by mouth or rectum in doses of 60 to 180 ml. of a 50 per cent solution or 5 to 10 ml may be injected intramuscularly It may be injected slowly intravenously in doses of 5 to 10 ml of a 25 per cent sterile solution

In birth injury, chronic encephalitis and posttraumatic convulsions *phenobarbital* is recommended while the *ketogenic diet* remains the treatment of choice for idiopathic epilepsy. High blood sugar decreases the 3 per second wave

and spike activity of petit mal epilepsy. After the convulsion, absolute quiet and bed rest for several days are prescribed. Wertheimer believes that placing the child in the ventral position, following delivery, acts as a prophylactic against the disastrous sequels (convulsions) of obstetric meningoencephalic hemorrhages.

German⁸³ states that the type of pathological lesion, while not without significance, is of slight aid in establishing a prognosis. Of 29 cases which he followed from 1 to 8½ years after surgical procedures, complete or partial relief from convulsive symptoms was secured in 19. The greatest proportion of satisfactory results was obtained from lesions in the parietal area. All patients should continue medication with phenobarbital for a considerable period after operation. Adequate medical treatment before resorting to surgery is imperative.

Sodium diphenyl hydantoinate (dilantin in America, epanutin in England) was recommended for the treatment of epilepsy by Merritt and Putnam 84 Its dose varies, depending on the therapeutic effects and toxic reactions. In adults, from 3 to 9 grains (0.2 to 0.6) Gm) may be given daily, while in children the dosage is started at 1.5 grains (01 Gm) twice daily and may be increased to 6 to 76 grains (04 or 05 Gm) until an optimum therapeutic dose is determined. If patients have been receiving large doses of bromides or phenobarbital, these drugs should be continued with the dilantin their dose being gradually reduced over a period of from 4 to 7 days. Sudden withdrawal of the bromides or of phenobarbital may precipitate a series of attacks before the reservoir of dilantin is built up. In special cases, when the attacks are known to occur at certain times, the drug can be administered so that the greatest concentration in the system is at that time. Noc-

turnal attacks may be prevented by giving most of the total dose before bedtime, and in women who are prone to have attacks at the time of their menstrual period an additional 1½ to 3 grains (0.1 to 0.2 Gm.) can be given on the critical days. Dilantin should be given along with the meal or afterward to avoid gastric symptoms. It is contraindicated in the elderly patient, those with hypertension or cardiorenal disease and in debilitated cases

Toxic reactions necessitating a reduction in dose are nervousness, tremors, or ataxia, giddiness, headache, hyperplasia of the gums, and epistaxis unrelated to ascorbic acid deficiency. The drug should be discontinued if severe dermatitis, purpura, or exfoliative dermatitis develop Dilantin is much less dangerous to life than bromides or phenobarbital, however, the drug should not be used except under the guidance of a physician When toxic symptoms develop, there is a slight progressive lowering of the red cell count and a proportionate fall in the packed cell volume without macrocytosis. A majority of cases shows a progressive fall in the blood sedimentation rate and except for an eosmophile increase, there are no alterations in the blood picture. Platelets are not diminished

Sufficient time has elapsed since the introduction of dilantin to permit a wide clinical trial. Merritt and Putnam claimed complete relief of grand mal in 58 per cent, petit mal in 35 per cent, and psy-

chomotor equivalents in 56 per cent. Improvement in behavior is striking. Irritability and violent episodes are diminished in frequency and severity. The patients are bright and alert and there is a subjective feeling of well being. The absence of a sedative effect proved undesirable. Its use among epileptic prisoners offers a new hope of assistance in rehabilitation.

Black⁸⁵ found that in 3 cases who did not tolerate over 6 grains (04 Gm) of dilantin, administration of 1/12 to 1/6 grain (5 to 10 mg) of benzedrine sulfate with the dilantin allowed a maximum of 9 grains (06 Gm) to be given without toxic symptoms Williams combined the administration of dilantin with bromides and phenobarbital and secured a 79 per cent reduction in the frequency of grand mal Pratt86 found that phenobarbital, in doses up to $4\frac{1}{2}$ grains (0.27) Gm), was not incompatible with dilantin and could be used in combination with it with benefit in cases where dilantin alone was meffective without toxic reactions

Prominal (N-methylethylphenyl barbituric acid) has been found superior to phenobarbitone in the control of convulsive and nonconvulsive manifestations in the majority of epileptics after 5 years' trial by Millman 87 The efficiency of the drug is not diminished when given over this interval but precautions are necessary to avoid renal damage. (Mebaral in America.)

MENINGITIS

By HENRY A DAVIDSON, MS, M.D.

Meningococcic Meningitis

Sulfanilamide and serum lowered the meningococcic meningitis mortality rate to 19 per cent in a series reported

by Campbell ⁸⁸ He recommends administration of serum by both intraspinal and intravenous routes Neal, ⁸⁹ however, questions the necessity of intravenous

serum medication in the absence of meningococcemia, preferring to limit this form of therapy to intrathecal injection. Campbell⁸⁸ administers the sulfanilamide by mouth unless the patient is vomiting. Neal's preferred sulfanilamide derivative is neoprontosil, which she finds "at least as effective and less toxic than sulfanilamide." Somers⁹⁰ prefers sulfapyridine, pointing out that even under adverse and primitive field conditions of medicine in North Africa, sulfapyridine lowered meningitis mortality from 75 per cent to 10 per cent.

Campbell⁸⁸ found that an average total sulfanilamide dose of 1 ounce (30 Gm.) per patient was sufficient in his group of successfully treated cases of cerebrospinal fever. The amount of serum necessary approximated 6% ounces (200 cc.) per patient. For sulfapyridine administration, Somers⁸⁹ recommends intraperitoneal rather than intramuscular injection. He uses 18 grains (1.2 Gm.) of the watery, or 45 grains (3.0 Gm.) of the oil suspension as the maximum dose for injection.

Streptococcic Meningitis

In the presulfanilamide era, streptococcic meningitis was practically 100 per cent fatal Toomey and Kimball,91 for instance, find a mortality of over 90 per cent in their 1935-1936 records, as contrasted with a death rate of only 16 per cent since they began using sulfanilamide They compute sulfanilamide dosage in the following manner. The dose is calculated as a grain daily per pound (140 mg per kg) of the patient's weight, with a maximum of 120 grains (8 Gm) a day This is administered in divided doses every 4 hours. As sulfanilamide is usually packaged in 5-grain (0.3 Gm.) tablets, it is not difficult to calculate a dosage schedule on this formula Thus, a patient weighing 100 pounds would receive a daily dose of 100 grains; that is, 20 5-grain tablets a day. This would then be administered in 4-tablet doses, every 4 hours, until the 20 tablets have been given. Kirstein⁹² prefers sulfapyridine to sulfanilamide, and cites a case of nonhemolytic streptococcic meningitis in which the patient almost died on sulfanilamide therapy, to be restored to health within 5 weeks after sulfapyridine had been substituted for the sulfanilamide.

Pneumococcic Meningitis

Prior to the introduction of sulfanilamide, pneumococcic meningitis was almost invariably fatal. Hewell and Mitchell.93 for example, reviewing their records prior to 1937, found a 100 per cent mortality. Since 1937, the death rate in their series fell to 50 per cent: an improvement which they ascribe to sulfanilamide. Hodes, Gimbel and Burnett⁹⁴ find a somewhat different prognosis. Their records indicate 100 per cent mortality without specific treatment; 94 per cent with sulfanilamide, and 53 per cent with sulfapyridine If patients moribund on admission are excluded from their calculation, the mortality rate for sulfapyridine-treated cases falls to only 21 per cent Neal⁸⁹ finds a mortality rate of 84 per cent in sulfamilamide-treated cases of pneumococcic meningitis. This more favorable outlook extends even to cases of otogenic origin, as indicated in recoveries reported by Gray and Adams,95 Silverstein and Thorner⁹⁶ (type III pneumococcic meningitis rising from a mastoiditis) and in recovery from a type VII case cited by Kreinin 97 The latter and Silverstein and Thorner96 used sulfanilamide. In the former case, prontosil (25 per cent solution) was used by mouth and sulfanilamide (08 per cent solution) by intraspinal injection.

Sulfapyridine dosage is calculated by Hodes, Gimbel and Burnett⁹⁴ on the

following basis. The daily oral dose is from 15 to 45 grains (1 to 3 Gm.) for children, 11/2 to 3 drams (6 to 12 Gm.) for adults. Full doses are given daily until clinical symptoms vanish and the spinal fluid remains sterile Oral medication should be supplemented by the intravenous injection of sodium sulfapyridine (a water soluble salt) prepared in distilled water in 5 per cent solution. The initial dose is 3/4 grain per pound (100 mg. per kg) of body weight A maintenance dose of 1/50 grain per pound (3 mg per kg) of body weight should be injected intravenously every 6 hours until the spinal fluid becomes sterile and clinical improvement is manifest.

Hemorrhagic Meningitis

Meningitis was the cause of bleeding in 6 of 52 patients with subarachnoid hemorrhage reported by Martinoff.98 In 2, the disease was tuberculosis meningitis, in 2 others, it was due to meningococci, in 1 to Staphylococcus aureus haemolythcus, and in 1 to the anthrax bacillus Xanthochromic fluid was found in 8 of 92 cases of tuberculous meningitis and in 6 of 63 cases of epidemic meningitis. In each case the bleeding occurred as a complication after onset of the illness. In the staphylococcic case, extensive infection of the walls of the vessels, with rupture, was demonstrated In the cases of bacterial meningitis, the number of white cells in the bloody spinal fluid was much greater than in the cases of spontaneous subarachnoid bleeding In hemorrhagic meningitis, the onset is usually with high temperature, whereas the temperature generally rises later in the course of subarachnoid hemorrhage While in most cases of meningitis the bleeding is due to direct injury and rupture of blood vessels, diapedesis may account for it in some instances.

Serous or Lymphocytic Meningitis

Incidence—Some idea of the incidence of lymphocytic meningitis is afforded by Skogland's survey⁹⁹ of the records of the University of Minnesota Hospital, in which an average of 1 case a year was found during the last 10 years. In only 1 of these 10 cases were antibodies against the virus found in the blood stream. In the other 9 cases, the diagnosis was based on the typical syndrome of meningeal irritation with spinal fluid lymphocytosis.

Diagnosis-Many workers including Lassen, 100 Oheim 101 and MacCallum and Findlay¹⁰² are impressed with the similarity between polionivelitis and serous meningitis Lassen, 100 in fact, believes that most cases of primary lymphocytic meningitis are of poliomyelitic origin The differences are that infantile paralysis is more seasonal, the initial spinal fluid cell count is higher in poliomyelitis (though by the end of the first week cell counts may be about the same), and the spinal fluid globulin, albumin and sugar are more likely to be increased in poliomyelitis. The best diagnostic criterion, according to MacCallum and Findlay 102 is identification of the specific neutralizing antibody. In most cases they find the virus in the nasopharynx for weeks after the onset of the illness. Skogland99 points out the coincidence of spinal fluid lymphocytosis with nuchal rigidity and headache as suggestive of this form of meningitis

Etiology—A virus in the upper respiratory passages is usually considered the focal source of lymphocytic meningitis. Armstrong and Sweet¹⁰³ believe that the gray house mouse is the chief carrier. They found the virus in mice trapped in the homes of 2 patients, whereas mice in houses in which no

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human cases had occurred were free of this virus.

Prognosis — The disease is usually considered benign, and is sometimes designated "benign meningitis." Weinberger, 104 however, reports a fatal case in which the illness persisted long enough to allow development of an obliterative arachnitis. Skogland and Baker 105 describe a persistent, chronic meningoencephalitis as a direct consequence of a lymphocytic meningitis. Oheim 101 found sequelae 8 years after the attack in 9 out

of 11 cases. These sequelae included headache, dizziness, emotional instability and, especially in children, conduct disorders.

Treatment—Repeated lumbar puncture remains the keystone of any treatment program. It is recommended by Molhant¹⁰⁶ along with hypertonic infusions of dextrose, intradermal tuberculin desensitization and roentgenotherapy. Skogland and Baker¹⁰⁵ tried sulfanilamide with some improvement in headache and nuchal rigidity.

MIGRAINE

By HAROLD D PALMER, M D

Recent studies lead to the conclusion that migraine headache should be looked upon as a manifestation of some pathologic functioning, the processes of which are retraceable from the actual headache to the vasomotor changes to the tissue toxemia and ultimately to certain causative agents thought to be by some investigators endocrine, by others allergic, by others inflammatory and by others ill-defined toxic accumulations in the tissues themselves. Whatever the etiological leanings of the investigators are the inherent (hereditary) predisposition toward a fixed pattern of reaction is not questioned. If we look upon the migrame episode as divisible into 3 stages, certain features of significance are revealed which help our understanding of the syndrome. The following train of events is suggested (1) The cumulative or premonitory stage (toxemia); (2) the stage of sympathetic nervous system imbalance resulting in the dilation of cerebral vessels (the headache), (3) the stage of elimination (recovery) 107

The allergists have much to say which warrants careful evaluation as to the na-

ture of the migraine episode as well as its etiology In writing of the whole migraineallergy concept. Hartsock and McGurl¹⁰⁸ have cleared up certain vague concepts which involve the allergic-emotional-sympathetic nervous system interaction in They believe that fatigue, the ailment nervous and emotional factors produce changes in the motor activities of the gastrointestinal system which result in duodenal stasis This promotes the absorption of the allergens to which the patient reacts in his inherent pattern of migraine They report that accurate allergy diets result in complete relief in 30 per cent of migraine patients and partial relief in 45 per cent. Other dietary management includes the low carbohydrate diet and the anti-retentional diet of Foldes 109 Studies of the vasomotor changes observed during migraine headache have been carried out by Graham and Wolff, 110 and Wolff and Sutherland111 and others and have led to some explanation of the mechanisms involved in the symptom of pain, and also of the mechanisms involved in the therapeutic effects of ergotamine tartrate and

other drugs. Pain in the migraine head-ache is apparently due to the stretch of relaxed (dilated) arterial walls, especially in branches of the external carotid artery. Reduction in the dilatation of these vessels and consequent relief of pain occurs upon the administration of ergotamine tartrate, either orally, hypodermically or intravenously. The oral dose usually given is 2 to 4 1/60 grain (1 mg) tablets, and that by hypodermic is 1/240 to 1/120 grain (0.25 to 0.5 mg.).

The success of any treatment depends upon the promptness of the administration after the appearance of the first symptoms of the attack Relief of headache can be anticipated in 60 to 70 per cent of cases The toxic effects have been somewhat discouraging but rarely alarming Von Storch¹¹² reports that the most commonly observed accessory symptoms are nausea, vomiting, numbness and tingling of the hands and feet, muscular pains and stiffness, choking sensations, feelings of substernal oppression, precordial pain, femoral or brachial perivascular pain and occasionally insomnia and restlessness. In the writer's experience these symptoms have been regarded as possibly disturbing to the patient but rarely of serious consequence. Only after larger doses are frequently repeated and if numbness, coldness and pain in the extremities become severe is there any danger of arterial thrombosis Oxygen inhalations have been suggested by Alvarez 11.3 The writer's experience with this method has been limited, but in a few instances relief has been obtained by prompt inhalation of 100 per cent oxygen and in 1 case prolonged improvement has followed consistent use Early use of this method may succeed in aborting attacks, but its value in prevention has not been sufficiently evaluated

There are various surgical procedures attempted in certain migrainelike neuralgic headaches. Craig¹¹⁴ reports 2 cases of hemicrania subjected to operation. In 1 patient the middle meningeal artery was ligated without benefit and later cervicothoracic sympathetic ganglionectomy was performed which resulted in complete relief. In another patient cervicothoracic sympathetic ganglionectomy and trunk resection resulted in complete relief from severe headaches of 17 years' duration Critchley 115 believes that Dandy's operation for removal of the stellate ganglion and ligation of the middle meningeal artery are sometimes justifiable in persistent cases of severe migrainelike pain and headache. Alcohol injections of the supra- and infra-orbital nerves and section of the trigeminal nerve have been recommended

Evaluation of endocrine and other therapies has been discussed by O'Sullivan¹¹⁶ who divided a large series of cases into therapeutic and symptom groups and from a study of these has presented a large amount of evidence to the effect that a placental extract (Emmenin) and estrogenic hormone (Progynon-B) with thyroid medication and other adjunct therapies wherever indicated have resulted in relief from the migraine syndrome. Dunn¹¹⁷ reports on the effect of testosterone propionate and estradiol benzoate in males suffering from migraine. He finds that 2000 R. U. of estradiol benzoate may be successful in aborting a migraine attack if administered at the onset of the symptoms and that a short series of injections of 5000 R U may prevent the recurrence of attacks for as long as 3 months in some cases subject to frequent migraine attacks Testosterone propionate failed to influence the course of the migraine in males. The rationale in the estrogenic

therapies would seem to be that these substances which have the property of inhibiting the production of prolan A of the anterior lobe of the pituitary prevent certain distortions of sympathetic nervous system functions.

Horton, MacLean and Craig¹¹⁸ have described a syndrome of vascular headache which has many resemblances to migraine, but which on close examination proves to be of different etiology and somewhat different in character. They have succeeded in reproducing the attacks of hemicrania or localized pain in the head and face by the subcutaneous injection of histamine phosphate in doses of 0.3 to 0.5 mg. Their method of treatment consists of subcutaneous doses of 0.05 mg of histamine twice each day for 2 consecutive days, then on the third day the dose is increased to 0066 mg twice daily which is continued until the fifth day when 0.1 mg twice daily is given. This dose is continued for 2 to 3 weeks in an effort to immunize the patient Definite, prompt relief has been obtained by them in 65 patients for periods varying from 2 weeks to 18 months

Recently the author has studied the effects of large doses of synthetic vitamin B_1 (thiamin chloride) in various combinations with liver extract and other vitamins in a series of patients suffering from severe migraine headaches

The results seem to indicate that some benefit can be anticipated both in the relief of the attack and possibly in the partial correction of some fundamental disorder of tissue metabolism which theoretically might lead to the vasomotor changes observed in the headache stage. The dose administered depends upon the severity of the disorder and in severe cases consists of an intramuscular injection of ½ grain (30 mg.) of thiamin chloride daily for 2 weeks, then 3 times weekly for a period varying from 2 weeks to 2 months, and then a gradual reduction in the frequency of dosage as warranted by the patient's response to the treatment. In refractory cases, liver extract is used in doses of 15 U.S P. units given intramuscularly once or twice weekly. Other vitamin therapy given concomitantly with the thiamin chloride and liver extract consists of oral doses equivalent to 30,000 U S P. units of vitamin A, 600 I. U. of vitamin B₁, 120 Sherman units of vitamin B_2 (G), 1500 I. U. of vitamin C and 3000 U S P. units of vitamin D. In addition to the relief from actual migraine attacks there is also considerable improvement in the general physical wellbeing of the patient. The use of this treatment has been too brief and the number of patients too few to warrant any statement as to its specific effectiveness, but further clinical testing seems justifiable

MULTIPLE SCLEROSIS

By Eli Marcovitz, M D

Etiology—During the past year there have been no striking developments in our knowledge of multiple sclerosis. By an investigation of the regional and occupational incidence of the disease, G. Steiner¹¹⁹ attempts to deduce the etiol-

ogy He states that a racial susceptibility has not been established, and that the geographical distribution both in the United States and Europe shows a higher incidence of the disease in the north than in the south. For example,

in New Orleans multiple sclerosis is a rare disease. The author also shows that the geographical distribution in the United States is the same for negroes and whites. He also points to the occupational predominance of woodworkers in Scotland, England and Germany. Familial cases of multiple sclerosis are mentioned, together with a new familial case of 2 sisters. He reports more fully a previously published case of conjugal multiple sclerosis and a new case which may also be conjugal From all the evidence he presents, the author deduces that these facts can best be explained on the basis of an infectious origin of multiple sclerosis

G B Hassin and I B Diamond¹²⁰ used the technic described by Steiner to demonstrate so-called "silver cells" and "spirochetelike" formations Steiner holds that these represent spirochetes and stages of degenerating spirochetes which he believes are the etiological agents of multiple sclerosis. However, the authors found these silver granules not only in multiple sclerosis but in many other degenerative processes in the central nervous system. They found that they were situated mainly between the axon and the myelin, were probably lipoids and denoted a metabolic disturbance of the central nervous system, an early stage of neural degeneration. The silver granules are present mainly in areas of extensive breaking up of the myelin, and their presence in multiple sclerosis confirms the view that this disease is of a degenerative and not of an inflammatory type. They conclude that Stemer's method is a valuable aid in demonstrating early stages of degeneration of the nervous system

Symptoms—M R. Brown and T. J. Putnam, 121 studied the occurrence of remissions in multiple sclerosis, and found only 41 cases, in a series of 133,

in which the disease was uninterruptedly progressive or stationary after a single attack Symptoms which are evidently due to small lesions, such as diplopia. central scotomata or sensory disturbances of a single extremity, tend to regress in a few months. On the other hand, symptoms which are apparently due to large lesions, such as paraplegia, ataxia or mental deterioration, are usually permanent. The authors found that isolated symptoms disappear in a far higher proportion of instances than do the same symptoms occurring in conjunction with others The first symptoms have a higher rate of recovery than the same symptoms occurring later in the course of the disease. Also, symptoms tend to grow more severe as the disease progresses

These facts suggest to the authors that most lesions of multiple sclerosis go through an acute stage, after which a variable number of fibers regain the ability to conduct impulses. Certainly in most large lesions, and probably in all lesions, there appears to be permanent destruction of the conductivity of some or many fibers.

Treatment—In discussing the criteria of effective treatment in multiple sclerosis T. J. Putnam¹²² points out that spontaneous remissions of greater or lesser degree occur in 69 per cent of cases. The first symptom of multiple sclerosis disappears completely in 44 per cent of patients. There is a higher incidence of remissions in office than in ward practice.

The author reviewed results reported with many forms of treatment and found improvement reported in 35 to 60 per cent of 1407 cases, with an average of 47 5 per cent. The effects of the more popular types of treatment in the present series, vis., high vitamins and liver extract, forced spinal drainage, arsphena-

mine, "germanin," typhoid vaccine, quinine and benzedrine, were not encouraging. The author concludes that the maximum extent of future recovery from acute lesions is determined at the time the lesions are formed, and that recuperative processes run their course irrespective of the treatment, aside from attention to general hygiene and nutrition. He believes that the criterion of the success of any treatment of multiple sclerosis probably should be not the induction of a remission but the prevention of relapses

O R. Langworthy¹²³ discusses the patho-physiology of disturbances in micturition in multiple sclerosis and suggests forms of treatment for the various types of disturbance. From a graphic study of bladder function in multiple sclerosis he concludes that there are 3 main types, with their possible combinations. Urgency is manifest in cases where efferent pathways from the brain are injured The stretch reflex is hyperactive, and the strength of the contraction waves gives rise to urgency An overactive stretch reflex empties the bladder more often. The symptoms in this type are urgent, frequent passing of small amounts of urine, with periodic incontinence On the other hand, hesitancy indicates a lack of strong contraction, due to mjury of the afferent pathways from the bladder to the cortex, or to injury of the cerebellum and its

pathways. Two factors lead to enlargement of the bladder. Sensory disturbance causes unawareness of fullness of the bladder. The bladder wall becomes passively stretched and there results loss of tone. Overdistention results in weakness of contraction and acute retention may supervene. Dribbling may be due to weak contractions of the wall or it may be due to overflow in acute retention. Incontinence is of several types:

1. With severe urgency, 2. periodic incontinence, 3 incontinence with acute retention.

The author recommends that hyperirritability be controlled by the administration of suitable doses of belladonna or atropine. Ephedrine combined with belladonna is even more efficacious. Even distention of the bladder with fluid may bring relief for a time. If there is a relaxed bladder and difficulty in initiating micturition, mecholyl by mouth is helpful, through its action on the parasympathetic The residuum of urine may be decreased or even eliminated by mecholyl, and the improvement may persist The dosage of mecholyl must be sufficient to produce physiological activity, $1\frac{1}{2}$ grains (100 mg) 3 to 4 times daily is recommended, and this is to be increased if it does not produce results Untoward autonomic symptoms may be controlled by the subcutaneous injection of atropine

MYASTHENIA GRAVIS

By George D Gammon, M D

Mechanism — Walker's discovery (1934) that eserme would relieve the weakness of myasthenia gravis revitalized studies of this disease and of related myopathic conditions. Coming just after the

development by Loewy and Dale¹²⁴ of the acetylcholine theory of the transmission of the nerve impulse, it aroused the interest of both physiologists and physicians in the possibility that a disturb-

ance of the acetylcholine mechanism might cause the weakness of myasthenia.

Under the Loewy-Dale hypothesis, each nerve impulse liberates at the nerve terminals a small amount of acetylcholine which in turn stimulates the muscle fiber to contract. This acetylcholine is almost instantly destroyed by an esterase in muscle and blood serum which changes it to the less potent choline and acetic acid. Eserine and its anlage prostigmine bind the choline esterase and thus free acetylcholine remains, with the result that repetitive contraction of muscle fiber occurs after each nerve impulse.

The effectiveness of eserine argued that in myasthenia either too little acetylcholine was formed, or that it was too rapidly destroyed. However, no excess of esterase, either in blood 125, 126 or muscle127 was found; therefore there was no indication of increased destruction of acetylcholine Indeed Lanari128 found an increased sensitivity of myastheme muscle, for amounts of acetylcholine which, injected intra-arterially, had no effect on normal muscle, caused a contraction in myasthema. This observation, as vet unconfirmed, leaves open the possibility but certainly does not prove, that too little acetylcholine is formed in invasthenia. It remains to be seen, therefore, whether the action of eserme in invasthenia implies an abnormality in the neurohumoral mechanism in this disease

Another analogy which has been stressed is the similarity of myasthenia to curare poisoning, since both are relieved by eserine Walker¹²⁰ reported evidence of a curarizing substance developing in myasthenic muscle during exercise; if the circulation was cut off from an extremity and the muscle exercised to fatigue, on readmitting blood to the part, distant muscles such as the

lids, became weaker. This observation has not been confirmed

Chemical studies of myasthenic muscle have revealed some abnormalities, the interpretation of which is not yet completely clear Nevin's review¹³⁰ covers the work. Both he and Reinhold and Kingsley¹³¹ found a high content of soluble ester phosphorus; the creatine content was normal. Cumings¹³² reported potassium in myasthenic muscle about twice normal; in one case the potassium decreased after prostigmine.

The large percentage of thymic abnormalities in myasthenia continues to stimulate search for the significance of the relationship Isaacson¹³³ reviewed the literature again and found 60 to 80 per cent showed some thymic abnormality Of 118 cases, 44 had tumors of the thymus, 27, hyperplasia; 18, persistence, and 22, no abnormality Several operators have reported improvement of the myasthema after surgical removal of the thymic tumors, but these results have been suggestive rather than conclusive The subject is reviewed by Blalock, et al 134 The most impressive claim is that of Adler¹³⁵ who produced a myasthenic condition in dogs by thymic implants This work has not yet been confirmed

Thorner¹³⁶ reviewed recently the relationship of thyroid disease to myasthema. In his case, and in others, as hyperthyroidism developed the myasthema improved

Diagnosis and Treatment—Marked improvement of muscular weakness by *prostigmine* is diagnostic of myasthemia gravis ¹³⁷ The dose should be adequate, ¹/₆₀ to ¹/₃₀ grain (1 to 2 mg.) hypodermically or ¹/₄ to ¹/₂ grain (15 mg to 30 mg.) by mouth Weakness due to other neural or muscular conditions responds very slightly, if at all, to the drug. Rarely the myasthemia case does not show a definite effect in all muscles, particularly

in the eye muscles, but the response elsewhere usually makes the result conclusive. In cases with little weakness the use of quinine aids in the diagnosis. Five grains (0.3 Gm.) t.i.d. for 1 to 2 days exaggerates myasthenic weakness, but does not affect other conditions ¹³⁸ Quinine should not be given to severe cases as there is danger of respiratory failure.

Schwab and Viets¹³⁹ treated 44 cases with prostigmine and other drugs; 7 had remissions, 5 died, the others were satisfactorily controlled. Although the percentage of remissions was slightly higher than expected, it is apparent that prostigmine is symptomatic treatment only.

Dosage requirements vary with the individual Schwab and Viets attempted to maintain a maximum prostigmine effect throughout the 24 hours. The dosage varied from 10 to 20 pills by mouth (15 mg) in the severe cases, down to 75 mg pills a few times daily in the milder cases. The pills should be given at the optimal intervals as determined by trial. They saw no increased tolerance or toxic symptoms from long-continued use. Others, however, have noted depressing effects from overdosage and a final failure to respond to the drug

For this and other reasons many physicians have not attempted to produce a maximum prostignine effect, but have reserved the drug for specific indications such as cough in respiratory infections, chewing meals, respiratory failure.

Minot 139 has introduced a new drug, guanidine, in the treatment of myasthenia. The action is longer than, but apparently not as marked as prostigmine. In Schwab and Viets' series less than a third of the cases responded to guanidine. Minot gave ½ to ½ grain per pound (13 to 28 mg per kg) of body weight by mouth or vein daily. If toxic

symptoms develop — nervousness, diarrhea, loss of appetite, nausea—the drug should be stopped; atropine sulfate or calcium controls the acute symptoms.

Of the other drugs employed in myasthenia, ephedrine, ¾ grain (50 mg.) several times daily, seems most useful. Potassium chloride, 75 to 150 grains (5 to 10 Gm.) orally, causes slight improvement in a few cases. Rest and adequate diet are still a mainstay. Glycine therapy has been disappointing. Prostigmine may be used to advantage combined with the other drugs mentioned

MYOTONIA

The mechanism of myotonia appears to be in some respects, particularly pharmacologically, the opposite of myasthenia gravis. The subject is reviewed by Harvey ¹⁴⁰. He and others observe an increase in myotonia from drugs which improve myasthenia, *i.e.*, prostigmine, potassium salts, and a decrease after quinine. There is no lowered serum choline esterase ^{125, 126} in this condition which might cause a faulty destruction of acetylcholine liberated by the nerve impulse. Some evidence points to an abnormality of the muscle itself, for myotonia remains after nerve block

Treatment—Quinine, introduced by Wolff, 141 relieves the myotonia by its curarizing action. The dosage is 5 to 10 grains (0 3 to 0.6 Gm) tid. This is valuable in Thomsen's disease, but in myotonic dystrophy, the myotonia rarely requires treatment as a symptom.

FAMILY PERIODIC PARALYSIS

The attacks of palsy in this condition are associated with a lowered serum po-

tassium.^{142, 148} The literature is reviewed by Gammon, Austin, et al.,¹⁴³ and Pudenz, et al.¹⁴⁴ Weakness can be induced by adrenalin, insulin, sugar, and water diuresis, all of which lower serum potassium. The depressed serum potassium in the spontaneous seizure is not due to a loss of potassium from the body, but a shift from serum to some other tissue, possibly the muscles. Potassium salts will cure the seizure in dramatic fashion.

Milhorat145 found a negative phos-

phorous balance in one case, but calcium and magnesium were normal.

Treatment—One and one-quarter to 2½ drams (5 to 10 Gm.) of potassium chloride by mouth will cure the seizure. To prevent attacks similar dosage is required. It must be given within a few hours of the seizure for otherwise it is eliminated and is ineffectual. In the author's case, 1 dram (4 Gm.) of potassium chloride was given at 4.30 A. M. daily with satisfactory control of the daily morning attacks

NEURITIS AND NEURALGIA

By Joseph C Yaskin, M D

The Guillain-Barre Syndrome

Three important clinical concepts seem to have evolved in the past few years in relation to multiple neuritis.

- (1) Many cases of multiple neuritis with different predisposing causes have as exciting and determining causes a state of vitamin deficiency, especially vitamin B₁
- (2) Multiple neuritis due to vitamin and other deficiencies is only a conspicuous part of the clinical picture in some cases and frequently there is associated involvement of the spinal cord and other parts of the central nervous system. In fact the lesions are often widespread and diffuse but are degenerative in character. Shattuck 146 and Austregesilo 147 offer comprehensive reviews of this subject.
- (3) Multiple neuritis is a conspicuous part of another central nervous disease, probably due to a virus infection. This was first described by Guillain, Barre and Strohl in 1916 who formulated the following criteria: onset suggestive of infection, more or less paralysis and sensory disturbances; high protein value

and low cell count in the spinal fluid, and good prognosis. On account of the favorable outcome, opportunities for studying the morbid anatomy have been rare, and attempts at bacteriologic study and at transmission to animals have not given any clue to the etiological factors A specific single virus or various infections may be responsible. Under the title "polyneuritis," Gilpin, Moersch and Kernohan have reported 35 cases, with 3 necropsies, which clearly belong to this group. There was at first a mild infection, followed after a latent period of days or months by a rather sudden onset of weakness or paresthesia in the extremities Facial paralysis was present in 35 per cent of the cases; choked disc, in 3 The protein content of the spinal fluid ranged from 100 to 800 mg. per 100 cc, and the average cell count was Necropsy in 3 cases revealed degenerative changes limited to the peripheral nerves, except for slight changes in the spinal cord in 1. Edema of the nerve bundles was a striking feature The other patients recovered in 6 months to 2

years. Facial diplegia, choked disc and partial spinal block have been noted by many other observers.

Bassoe¹⁴⁸ reports 3 cases with a much more varied and alarming clinical picture than that of the Guillain-Barre syndrome, but all had an onset suggestive of infection, a high level of protein in the spinal fluid and a favorable outcome.

The pure syndrome of Guillain-Barre is explained by lesions of the peripheral nerves, nerve roots and spinal meninges. Other features may be superimposed. The clinical picture may be dominated by brain, spinal cord and cranial nerve symptoms and may be exceedingly alarming, but the 3 cardinal features of the Guillain-Barre syndrome remain. Anatomically, in the pure syndrome there is meningoradiculoneuritis; when the spinal cord or the brain are also involved, longer terms are required, such as "meningomyelo-encephalitis" and "meningomyelo-encephalitis"

Polyradiculoneuritides with albuminocytologic dissociation and favorable evolution (the Guillain-Barre syndrome) may occur in epidemics Such an epidemic is reported by Ludo von Bogaert, et al 149 The fact that they observed 9 typical cases of the syndrome in 4 months and 2 more later, not counting 10 abortive cases, showed that this was an epidemic group of cases of a disease described mostly as sporadic The opinion of some colleagues that these cases might be radiculomeningeal forms of infantile paralysis led to a comparative systematic study of the evolution of the cerebrospinal fluids and of the electrical reactions of a group of polyradiculoneuritides, 1 of typical poliomyelitis and 1 of the other polyneuritides presenting dissociation of albumin and cells but having a different evolution. The group of polyradiculoneuritides occurred especially in July and August, that of poliomyelitis in August and September and that of insufficiently established radiculoneuritides and of neurotropic infections in all the summer months.

In each of the 9 cases the onset was of infectious origin, often with apyrexia or slight fever. There was a 2- to 8-day interval between the infectious onset and the appearance of the first meningoradicular symptoms. The initial temperature curve and the intense meningeal reaction extending to the entire spinal cord recall certain forms of acute poliomyelitis. Opisthotonos may persist for weeks, is usually localized to the dorsal part of the spine and is accompanied by intolerable pain in some cases and by paresis extending to 1 or more extremities. This diffuse primary extension of the paresis which persists during the stationary phase is striking. Superficial sensory disturbances are slight, while deep sensory disturbances occur and explain in part the ataxia in these patients. Vasomotor and trophic disorders, not mentioned by Guillain and Boudin, always present The ataxia is pseudotabetic; it may be of the polyneuritic or cerebellar type, consequently the possibility of a cerebellar phase, although unexplainable in a meningoradicular disease, should be remembered In the stationary phase the paretic disturbances are found especially in the distal parts of the limbs, although the reverse may occur, recalling the myopathic distribution, and it has been demonstrated that certain pseudomyopathic polyneuritides of children belong to the Guillain and Barre type Facial diplegia during the disease has been reported prior to the present study The presence of the cerebrospinal syndrome is essential for diagnosis, albuminosis may reach high values and persist for a considerable time. The electrical reactions show that the nerves and

muscles are affected practically symmetrically and that all those of the lower extremities and sometimes also of the arms and of the face may be involved, degeneration being usually incomplete.

Differential Diagnosis-Differential diagnosis between these polyneuritides and infantile paralysis may be difficult, especially when the latter appears under a form simulating Landry's syndrome or under a meningeal and painful form. However, the evolution curve of the cerebrospinal fluids of the 2 diseases shows decided differences The group of polyradiculoneuritides, which was contemporaneous with the other group but was insufficiently studied or presented an incomplete biologic syndrome, seems nevertheless to belong to the Guillain and Barre type, while the contemporaneous nonclassifiable neurotropic infections and some polyneuritides of known or unknown etiology, presenting a chronic evolution with albuminocytologic dissociation, do not

The authors conclude that the disease described by Guillain and Barre in 1916 is an entity, probably of intectious origin, evolving taxorably and without sequels in most cases. Although they cannot prove it they think that the disease is caused by an autonomous virus. Among the confused group of polyneuritides described in the literature, it constitutes a type interesting from the prognostic point of view and for which they accept the term "polyradiculoneuritis with albuminocytologie dissociation and favorable evolution" because it presents the essential symptoms. This does not mean that there are no polyradiculoneuritides with favorable evolution but without albuminocytologic dissociation, that fatal cases cannot be found in Guillain and Barre's disease, or that any polyneuritis evolving favorably or with recurrence and presenting albuminocytologic dissociation necessarily belongs to this group; in the clinical evolution in typical cases the curve must be taken into account. There are undoubtedly cases that cannot be classified, such as certain complex cases described under Landry's syndrome

Peripheral Nerve Lesions in Pernicious Anemia

It has been recognized for several years that serious gastric disturbances, especially carcinoma of the stomach, may cause a polyneuritis due to a deficiency state An additional convincing case is reported by Laurent and Sinclair¹⁵⁰ in a 32-year-old man suffering from a pyloric carcinoma. That neuritic changes are common in permicious anemia is not generally appreciated.

Van der Scheer and Koek¹⁵¹ point out that attention has been given chiefly to the changes in the spinal cord associated with pernicious anemia, particularly to those of the long ascending and descending tracts in the posterior and lateral columns

Most of those who have studied permeious anemia regard the involvement of the peripheral nerves as ex-There are, however, some investigators who have described cases in which polyneuritis is found alone or together with medullary changes, and a few accept the view that it is the rule that polyneuritic symptoms are part of the clinical picture of the disease. The observations which the authors made in 38 cases of permicious anemia convinced them of the correctness of the view of the latter investigators. The smooth tongue, with tenderness at the tip and oversensitiveness to heat and acidity, which is one of the most important symptoms of permicious anemia, is the result of degenerative changes in the nerves innervating the tongue. In view of this fact, it is remarkable that practically

identical symptoms in the tips of the fingers and toes, the paresthesias, the severe pains and the supersensitiveness to cold and heat are ascribed not to neuritis but to a central medullary proc-Moreover, it is surprising that it is never considered strange that in a disease implicating the entire organism the nerves of the tongue should be the only part of the peripheral nervous system to be regularly attacked. In the 38 cases of pernicious anemia described by the authors, the patients without exception complained of numbness and tingling in the distal ends of the extremities. These symptoms gradually increased in intensity, spread toward the knees and elbows and occasionally passed toward the trunk. The authors do not agree with the statement of many investigators that impairment of cutaneous sensitivity occurs only in advanced stages They give detailed clinical histories in some of the cases observed by them However, they do not regard it sufficient to offer clinical evidence, so they also furnish histologic observations. Although the number of cases in which anatomicopathologic proof of impairment of the peripheral nerves was obtained is limited, they lend strong support to the view that, in addition to the medullary lesion in the cord, the system of the peripheral nerves is also seriously involved in pernicious anemia

Tick Paralysis Due to Bite of the American Dog Tick

Robinow and Carroll¹⁵² report a case of ascending flaceid paralysis in a child of 7 years

Weakness of 1 week's duration had progressed to a flaccid paralysis of the legs, weakness and asynergia of the arms, thick speech and nystagmus. All laboratory determinations were normal, including blood counts, urine, spinal

fluid serology and stools. Two ticks, identified as the dog tick (*Dermacentor variabilis Say*), were found on the scalp and removed Improvement began at once and was complete in a week.

The following course is regarded as typical: rapid development of an ascending type of paralysis; the finding of ticks, rapid recovery after removal of the ticks. Death is to be expected if the ticks are not removed. The cause of the paralysis is supposed to be a venom elaborated in the ova of impregnated female ticks. The disease occurs mostly in children and young animals, rarely in adults. It has been found in the western part of North America. Although the dog tick is common in the east, this is the first human case reported east of Wyoming.

Syphilitic Polyneuritis

Polyneuritis in the course of syphilis is not rare but is usually ascribed to the agents used in the treatment of syphilis, especially the arsenicals, or to associated conditions such as alcoholism, deficiency states, and other intoxications or infections Rarely the multiple neuritis may be due solely to syphilis Such a case is reported by Simon and Berman. 153 At autopsy the pathologic changes in the peripheral nerves were characteristic of syphilitic infection. The authors state that syphilitic neuritis may occur in any stage of syphilis and that the prognosis is favorable if early, regular and sufficient antisyphilitic treatment is instituted

Horse Serum Neuritis

Bennett¹⁵⁴ reports 5 cases and collected 115 in the literature. Most of the reported cases were in young adult males, with half following prophylactic tetanus antitoxin. Since most cases develop from industrial injuries requiring prophylactic tetanus antitoxin, they present economic and medicolegal problems.

Neurological signs and symptoms of serum sickness may be meningeal, cerebral, or referable to the spinal cord, but the most common reactions occur in the peripheral nerves, usually affecting here the upper brachial plexus and the roots of the fifth and sixth cervical nerves.

Radial paralysis is infrequent. Bennett reported 1 case, while Angelesco, Popovici and Balutza¹⁵⁵ reported another case and collected 4 from the literature.

The 4 theories of the pathogenesis of serum neuritis are: (1) Direct toxic action of the serum; (2) selective action of toxins on nerves with low chronaxias; (3) compression from perineural edema of sheaths about the intervertebral foramina or bony grooves, and (4) vascular origin—nerve cell death from vasodilation, perivascular infiltration, and hemorrhage

The symptoms of neuritis occur at the height of the serum sickness, with severe pains in the neck, shoulders, arms, or legs, unrelieved by analgesics or opiates Within hours to a few days, flaccid paralvsis develops, followed by muscular atrophy with muscle tenderness and dull pains, persisting for weeks. Motor paralvsis, atrophy anesthesia, reduced reflexes, and at times fibrillations occur, depending on the segments involved, usually the suprascapular and axillary nerves are affected unilaterally patients recover within 6 months, some take as long as 18 months. About 20 per cent are left with some residual atrophy and weakness, mainly in the deltoid There is no known method of muscle preventing serum sickness unless other animal serum antitoxins can be substituted for horse serum. Tetanus alumprecipitated toxoid might prevent teta-The justified but more scientific administration of tetanus antitoxin might reduce serum sickness

On recognition of the early symptoms of neuritis, immediate treatment is recommended. Repeated injections of adrenalin, dehydration, and fever therapy. hot baths, followed by pilocarpine blanket packs or the administration of artificial fever at 103° to 104° F. (39.5° to 40° C.) for 2 to 3 hours daily for several treatments, may prevent severe atrophy. After the stage of serum sickness, the treatment is largely symptomatic: immobilization of the arm in an abduction splint, general nutritive and vitamin therapy, local and general heat to relieve pain and hyperesthesia and physiotherapy in the form of massage and electric stimulation

Nerve Injuries Caused by Intravenous Injections of Dextrose

Hassin¹⁵⁶ reports 8 cases of injury to the large nerve trunks of the upper extremity following intravenous injections of dextrose. In 5 cases the median nerve was involved and in 3 the median, musculospiral and ulnar nerves. In 1 case. paresthesia was still present about 3 vears after the injections. The instructive features of these cases are the predominant involvement of the median nerve, the prevalent lesion of the sensory nerve fibers, the long duration of the anesthesia and the obscure mechanism of origin of the lesions There is no doubt that they are due to the injections, but it is questionable whether they are caused by nicking of the nerve by the needle; the median nerve is nearer the cubital veins than the other nerves. The presence of ecchymoses around the elbow in 2 cases suggests such an etiology, although pressure by adhesive plaster holding the needle in place on the arm or the arm's fixation against the board combined with the long duration of the injections in debilitated patients may also be responsible

The edema and swelling present in some cases can hardly be considered contributing factors as swelling was absent in other cases. Probably several factors are instrumental in the causation of the nerve lesions.

Pressure on Brachial Plexus Causing Simulation of Coronary Disease

Painful conditions about the shoulder and evidences of brachial neuritis are not usually primary in origin. More frequently such conditions are due to periarthritis and bursitis of the shoulder region, radiculitis and vertebral and spinal cord disease Less frequent causes include superior sulcus tumors (q v.) and metastatic tumors of the upper part of the lung (Miller, Frugoni and Craig). ¹⁵⁷ The rôle of a cervical rib and of the scalenus anticus muscle in the production of symptoms is often forgotten ¹⁵⁸

Reid¹⁵⁹ observed a series of patients in whom the pressure of a cervical rib or the scalenus anticus muscle on the brachial plexus had been the cause of pain simulating angina pectoris. These diagnoses differ significantly in prognostic and therapeutic implications. The syndrome has been found in the absence of a cervical rib, in such cases, an abnormality in the relation of the first rib and the brachial plexus is the cause syndrome has been explained as due to friction neuritis; the nerves are made taut across the sharp edge of the rib as the result of various unfavorable conditions in the relations of the nerves to the bony structures. More recently, attention has been directed to the effect of the scalenus anticus muscle in causing pressure on the subclavian artery or brachial plexus or both The scalenus anticus muscle may compress the artery or nerves against the cervical rib, if such is present, or it may abnormally elevate

the first rib and so interfere with the artery and plexus. If the latter is irritated, the scalenus anticus muscle, which receives its innervation from the brachial plexus, may be stimulated to a state of spasm. A "vicious cycle" may be said to exist. The important part played by the scalenus anticus muscle and the fact that it may cause symptoms identical with pressure by a cervical rib, in cases in which there is no extra rib, are the justification for the term "scalenus anticus syndrome" Pain, paresthesia, and anesthesia in the area supplied by the affected nerve are the usual symptoms. The pain is neuralgic in character: it may begin in the neck and spread downward along the arm to the hand and sometimes in the reverse direction to the head and side of the chest Rotation of the head toward the affected side or a downward pull on the shoulder may increase the pain. Loss or decrease in amplitude of the radial pulse and a bruit over the clavicle are other symptoms and signs that may be noted. The simplest form of treatment is that of elevation of the shoulder upward and backward by a Physical therapy is then used in an attempt to develop the trapezius and levator anguli scapulae muscles If such measures prove unsuccessful and the symptoms warrant it, surgical treatment is advised. Operations are described for removal of the cervical rib or first rib, whichever is the cause of the pressure on the brachial plexus or subclavian arteries. A considerable number of patients have been relieved by section of the scalenus anticus muscle without removal of the bone

Median Thenar Neuritis (Partial Thenar Atrophy)

This is an uncommon condition characterized by weakness and atrophy on the outer side of the thumb unaccom-

panied by sensory disturbances or reflex changes, and a tendency to become spontaneously arrested. The condition may be confused with the early symptoms of syringomyelia, progressive muscular atrophy, amyotrophic lateral sclerosis, spinal cord lesions, brachial neuritis, cervical rib, and occupational neuritis. Moersch¹⁶⁰ and Wartenberg¹⁶¹ report cases and discuss the etiology, clinical course, and treatment of this condition.

Moersch reports a case of a 39-year-old woman with weakness associated with muscular wasting on the outer side of the thumb. Five years earlier she had fallen on her right hand, but this incident was seemingly unrelated to the present condition, the onset of which occurred 9 months prior to examination and which was manifest as clumsiness and weakness of the right thumb in executing the finer movements and in writing. An increased wasting of the muscles on the outer side of the right thumb was noted, and definite atrophy was evident in a few months. Similar symptoms developed in the left thumb 6 months after the initial symptoms.

The process had seemingly halted in the right hand but was still progressing in the left. There had been no associated pain, numbness, paresthesia or fibrillary twitching. General examination was negative. Neurologic examination revealed nothing abnormal except the findings associated with the hands. All the deep reflexes of the upper extremities were normal. Sensation was undisturbed. During the ensuing 6 months the weakness and atrophy of the left thumb progressed so that both thumbs were similarly affected. Four years, later, the patient was continuing her stenographic work, but the condition remained unchanged.

The syndrome presented by this patient, although not common, is very characteristic and when once it is understood, is recognized readily. The condition has been referred to under different titles by various writers. It appears most commonly in the later decades of life, affects both men and women and may be unilateral or bilateral. As a rule, the syndrome develops spontaneously, although there

may be a history of some injury, inflammatory process, or prolonged occupation trauma, producing what may be termed a tardy median thenar neuritis, in contradistinction to an acute median thenar neuritis which develops rapidly as the direct result of trauma to the median nerve in the hand The explanation for the development of this specific form of median neuritis is probably on an anatomic basis The median nerve as it passes under the anterior annular ligament of the radius gives off the thenar branch which is entirely motor in its function. This branch which passes to the muscles affected, is capable of producing only a motor paralvsis It is likely that the thenar branch, as it emerges under the annular ligament and then swings backward and outward to the muscles, is compressed either by direct trauma or by continued irritation In some instances, paresthesias and even sensory changes are to be observed in the affected area These sensory disturbances probably are attributable to an involvement of the main trunk of the median nerve at the annular ligament or to injury of a sensory median twig which may be given off at that point. Median thenar neuritis may be either acute or tardy. It does not progress beyond the affected area. In cases in which the atrophy has been present for a considerable period of time, the possibility for return of function is remote. In the early stages of development of the atrophy relief may be obtained by removal of irritating factors or by surgical measures, such as relieving pressure on the thenar branch of the median nerve by section of the anterior annular ligament It is important to recognize this syndrome, as an incorrect diagnosis of progressive muscular atrophy, tumor of the cervical portion of the spinal cord, cervical rib, or neuritis of the brachial plexus and so forth often is made, indicating a much

graver prognosis than the diagnosis of median thenar neuritis.

Delayed Paralysis of Nerves from a Single Muscular Contraction

The etiological diagnosis of mononeuritis, except when resulting from direct trauma, compression, or from infectious or toxic causes, is often difficult. It is generally known that indirect trauma. including severe muscular contraction, may cause a neuritis. Nielsen¹⁶² reports 5 cases in which paralysis of peripheral nerves resulted from a single muscular contraction and stresses the fact that the appearance of the paralysis may be delayed In 3 of these cases there was an involvement of the common peroneal nerve, in 1 the long thoracic nerve, and in I several branches of the cervical plexus

Nielsen believes that delayed paralysis from a single muscular contraction may result from such action as a stumble, a sudden reaching forward or a sudden thrust of the hand upward for the purpose of regaining one's balance, the etiology is easily overlooked and in industrial work the industrial nature is often not conceded

It is quite probable that more than 1 type of etiology may be concerned in such cases, e/g, intoxication, general anesthesia, or chilling, but the muscular action with resultant contusion of the nerve is the exciting cause

To avoid the danger of ascribing any obscure paralysis of a nerve to hypothetic muscular action, it is suggested that for a given case to be valid as belonging to this group there must have been (1) some sort of sensory discomfort in the affected area at the time of the injury, (2) continuance or recurrence of the discomfort for hours or days, (3) possibility of compression of the affected nerve

by the muscular contraction assumed responsible, and (4) appearance of paralysis within, say, 2 months of the strain.

Painful Conditions of Lower Extremities and Back

Pain in the lower limbs and back still remains a difficult diagnostic and therapeutic problem. While some observers still look upon most sciatic syndromes as infectious in origin, others, especially in America, find operable mechanical causes to account for many painful conditions in this region.

Lumbosacral Neuritis -- Pette and Becker¹⁶³ attempt to reclassify the inflammatory diseases of the peripheral nervous system. They regard sciatica as a well circumscribed disease and prefer to call it lumbar or lumbosacral neuritis, according to the distribution of its symp-This study is based on a survey of 30 selected cases. 9 of which are reported in detail In addition to the customary symptoms, which may be equivocal in some cases, the authors point out the presence of vegetative signs, such as coldness or pallor of the limb involved, hypohydrosis and edema Objectively, they find increase of cells and protein in the lumbar spinal fluid, frequently with a pathologic mastic curve and a decreased albumin-globulin ratio Changes in the bones or joints are not recognized as causative factors. Morphologic changes have never been reported. They believe that the etiologic factor may be a virus related to herpes zoster and that the inflammatory process is probably located in the spinal ganglia

Protrusion of the Intervertebral Discs and Hypertrophy of Ligamenta Flava—The importance of the posterior protrusion of the interverbral disc as a cause of low back and sciatic pain is attested by the report of 300 cases from

the Mayo Clinic by Love, ¹⁶⁴ of 83 cases from the Massachusetts General Hospital by Barr, ¹⁶⁵ and by a large series of cases by Spurling and Bradford, ¹⁶⁶ and others.

According to Walsh and Love, ¹⁶⁷ who report 200 cases, the protrusion occurs 3 times more commonly in men than women. The great majority of the protrusions occurred in the fourth and fifth lumbar discs. A few protrusions occurred in the dorsal and cervical regions. Of the 200 cases, 21 had multiple protrusions. In only 73 cases was there a history of injury preceding the onset of the symptoms

A characteristic feature of the syndrome is the remarkable intermittency of the symptoms which was noted in 180 out of the 200 cases. During the interval between attacks, the patient may feel well, although frequently some residual ache in the back, paresthesia or muscular weakness may remain

Protruded disc in the cerucal and dorsal regions give symptoms and signs more or less characteristic of extradural tumors in these regions, but the pain has a tendency to appear intermittently in cases of protruded disc

Protruded disc in the lumbar region gives rise to the following manifesta-Sciatic pain, usually unilateral, accentuation of the pain on coughing and sneezing; night pain occurring in about a fourth of the cases and paresthesia in about half the cases. Low back pain existed and preceded extension of the pain in 112 cases, whereas in 40 cases low back pain and sciatic pain appeared simultaneously In only 9 cases did the sciatic pain precede the onset of low back pain. In only 10 cases did the patient complain of sciatic pain alone without low back pain, whereas in 6 cases the extension of pain was not along the sciatic nerve It should be emphasized

that a patient complaining of a bizarre extension of pain in all probability does not have a protruded intervertebral disc. The commonest physical signs of a protrusion in the lumbar region are (1) a positive Lasegue sign or straight leg raising sign; (2) sciatic tenderness, and (3) diminution or absence of 1 or both Achilles tendon reflexes. In a smaller number of cases, segmental impairment or loss of sensation, muscular paresis, relaxed anal sphincter, and diminution or loss of the hamstring or patellar reflexes occur. In 33 cases the only finding on neurologic examination was a positive Lasegue sign or sciatic tenderness, and in 12 cases the neurologic examination gave objectively negative results Thus, an essentially negative neurologic examination does not exclude the presence of a protruded intervertebral disc. In most cases, the normal lumbar lordosis has been lost, and in many a reversal of the normal lumbar curve associated with a prominence of the spinous processes of the third, fourth, and fifth lumbar verte-Involuntary spasm of the brae occurs muscles limits all motions of the back. but hyperextension is usually particularly painful. The patient often has a pronounced list to one side on standing, the trunk is thrust forward and to 1 side to avoid placing the full weight on the painful leg A limping gait is often noted owing to these factors and, in some cases, to actual muscular weakness

According to Naffziger and Jones, 168 sustained pressure over both jugular veins reproduces or exaggerates the sciatic pain. This usually occurs in patients who have pain on coughing or sneezing

Spinal fluid studies should be performed in any lasting low back and sciatic pain. In the cervical and dorsal regions, Walsh and Love¹⁶⁹ found subarachnoid block in half and protein in-

crease in two-thirds of these cases. In the protrusions in the lumbar region, the total protein was over 40 mg. per 100 cc. in 66 per cent of cases.

Although Walsh and Love,167 Spurling and Bradford, 166 and others with wide experience feel that protrusion of the intervertebral disc in the lumbar region can be diagnosed by the characteristic symptoms and signs, in the great majority of cases, the final diagnosis and localizations depend on x-ray studies after the injection of a contrast medium, such as lipiodol or air. All observers agree that no x-ray studies by the aid of a contrast medium should be performed unless and until a careful clinical study justifies such a procedure. Most clinicians feel that lipiodol may have unpleasant sequelae, although Spurling and Bradford¹⁶⁶ and others have seen no lasting ill effects. Air injections thus far have not been uniformly reliable, although Chamberlain and Young¹⁶⁹ based on a study of 300 spinograms consider the method reliable and harmless.

Hypertrophy of the Ligamentum Flavum — According to Camp¹⁷⁰ and Love, ¹⁶⁴ this condition has been found frequently by neurosurgeons in conjunction with a protruded intervertebral disc It generally occurs at the same level as the protrusion but may occasionally be found at other interspaces. Localized hypertrophy of the ligamentum flavum without coincident protrusion of a disc is not common, but when it does occur it may imitate all the clinical phenomena of a protruded intervertebral disc

The *treatment* of protrusion of intervertebral disc and hypertrophy of ligamentum flavum is always surgical. Most neurosurgeons perform a *laminectomy* but Love¹⁶⁴ has been successful in some cases with a *hemilaminectomy*. When hypertrophy of the ligamentum flavum is

found, the ligament as well as the protruded disc is removed. Bone grafts were not found necessary.

The end results of these cases, according to the statements furnished by many observers, are most satisfactory. Most of the patients get complete relief, and the others marked improvement.

Meralgia Paresthetica (neuritis of the lateral femoral cutaneous nerve)-Based on a study of the records of 150 patients, Ecker and Woltman¹⁷¹ state that the chief symptom of meralgia paresthetica is a sense of numbness over the anterolateral aspect of 1 thigh (22 per cent of patients had bilateral symptoms). Later are added burning, tingling, and pain, aggravated by standing or walking. There may be slight loss of appreciation of light touch, pain and thermal sensation in the affected area. This clinical syndrome was caused by (1) primary lesions within the spinal canal, such as multiple sclerosis, (2) residuum of radiculitis, (3) osteitis of the second and third lumbar vertebrae, (4) complication of spinal anesthesia, (5) hypertrophic arthritis of the lumbar vertebrae, (6) intraabdominal and intrapelvic conditions, such as lesions of the appendix and cecum, rapid abdominal enlargement due to tumor, and pregnancy, (7) injury to the lateral femoral cutaneous nerve as it passes through the fascial canal in the upper part of the thigh, and (8) abdominal compression due to trusses, belts, and corsets

Most patients required no treatment, there being spontaneous disappearance of symptoms. An offending belt or truss should be removed or padded. Other forms of treatment were resection of the nerve and neurolysis. The authors conclude that meralgia paresthetica is a neuritis of the lateral femoral cutaneous nerve which most frequently affects obese middle-aged persons

Relief of Neuritic Pains by Artificial Fever Therapy

Bennett and Cash¹⁷² have used the hypertherm for the induction of artificial fever in a large variety of diseases. Up to January 1, 1937, in 26 months, they treated 581 patients, who received more than 2650 fever treatments. Of these patients, 40 underwent fever therapy in an attempt to obtain relief from severe neuritis, myalgia, or a radicular painful state. There were 20 patients with sciatic neuritis, 6 with brachial neuritis, 5 with toxic-infectious polyneuritis and infective neuronitis. 3 with herpes zoster, 2 with lymphocytic meningitis, and 4 with miscellaneous arthritic states with secondary neuritis or neuralgia All types of neuritic pain were relieved immediately, but pain recurred in some cases, especially in those of secondary neuritides resulting from compressive lesions This form of heat therapy (with temperatures from 103° to 105° F - 395° to 405° C) is a distinct advance over all forms of local use of heat in relieving pain. Fever therapy is recommended not as a substitute for other accepted forms of therapy for neuritis but only as an aid in the management It probably hastens convalescence in the severe toxic-infectious polyneuritic states The physiologic mechanism by which general fever induction effects relief from neuritic pain is not well understood Undoubtedly, the enhanced blood flow and peripheral vasodilatation in the inflamed areas increase tissue oxidation and nutrition Leukocytosis, phagocytosis, and mobilization of immune bodies secondary to induction of fever play a part in the absorption of deposits occurring in rheumatism, dilution of toxins, and the healing of inflamed nerve tissues. The treatments do not interfere with any other indicated therapy and are

practically without danger in experienced hands.

The "Cervical Group" of Facial Neuralgias

It is well known that a number of painful affections of the face other than the major trigeminal are extremely resistive to any form of treatment. In a considerable proportion of these cases. Tosef Wilder¹⁷³ found not only that there was a clinically and roentgenologically demonstrable deforming spondylarthritis of the cervical vertebrae but that attacks could be interrupted or induced by forced movements of these vertebrae. Prompt therapeutic results can be obtained with diathermy or mud baths to the neck and with subcutaneous injections of about $2\frac{1}{2}$ drams (10 cc.) of a 0.5 per cent novocain solution over the spinous processes of these vertebrae. As most patients with neuralgia of the face suffer from frequent spasms which begin and end with the attack of neuralgia, the relation of "crampus disorders" to blood uric acid was investigated. Values above 4 mg per cent were found in many

Of 17 patients, 9 showed spondylarthritis, cramps, hyperuricemia, and a positive response to the combined spondylarthritic and antiuratic treatment Six did not suffer from cramps, in 2 of whom proof of therapeutic response was uncertain Another had no hyperuricemia. and in 1 the cervical column was not examined roentgenologically (it was clinically normal) In 8 of the 17 patients there was radiation of the pains over the region innervated by the trigeminal nerve, mostly to the back of the head and behind the ear, and encroachment of disturbance of sensibility into the domain of the cervical nerves In the histories of 10 of the 17 patients there were slight polyneuritic symptoms.

The usual antiuratic treatment is used. The spondylarthritic treatment consists in keeping the *head at rest* as much as possible (dorsal position at night with a round pillow to support the neck);

diathermy 3 times a week up to 30 to 40 applications; novocain injections up to a maximum of 10, between diathermy sittings. Instead of diathermy, mud applications may be used.

PARALYSIS AGITANS

By Eli Marcovitz, M.D.

Treatment — During the past year there has been further discussion of the relative merits of the "Bulgarian treatment" as compared to other forms of treatment with belladonna and similar drugs.

H. Roger and J. E. Paillas¹⁷⁴ report excellent results with the use of the Bulgarian treatment. They employ a 5 per cent decoction in white wine of the belladonna root grown in the Balkans. Beginning with a dose of 10 drops, tid., they increase the dose daily by 5 drops at each dose, up to a dosage of 180 to 200 drops, which is then given in 2 divided doses. This dose can then be reduced to find "the smallest quantity of drug giving the maximum amelioration with the minimum of (untoward) incidents" The authors recommend that on 4 or 5 days during every month only half of the dose should be taken, to permit elimination of the toxin. Also, once a month there should be complete discontinuance and the administration of a saline purge They strongly recommend daily exercises, especially for the hands, to increase suppleness Severe cases should be hospitalized for the treatment, but the less severe cases can remain ambulatory

They obtained very excellent results in all types of parkinsonism, whether or not they were postencephalitic in origin Furthermore, they reported excellent results in all postencephalitic syndromes, especially in the akinetic-hypertonic type. However, on other extrapyramidal syndromes, viz, athetosis, torticollis, Huntington's chorea, hemiballismus, and in pyramidal contractures and epilepsy, the treatment had no influence.

Serious contraindications to the treatment are poor renal elimination, prostatism or cardiovascular disease

The authors also discuss the management of complications of the treatment. For severe buccal dryness they recommend chewing gum Special glasses are sometimes prescribed for the paresis of accommodation. Various laxatives are employed for constipation. When this complication reaches the state of intestinal stasis the treatment is stopped, and prostigmine and pituitrin are used, with an oil lavage. Vomiting is considered evidence of a massive intoxication

In general, the authors recommend a diet high in cellulose, and limitation of alcohol and condiments.

D. Hill¹⁷⁵ compared the effect of decoctions of the Bulgarian and of the English belladonna root on 14 patients with parkinsonism and found no appreciable difference in the action of these 2 preparations

By means of graphic methods N. S. Alcock and E. A Carmichael¹⁷⁶ studied the effects of Bulgarian belladonna root, English belladonna root and stramonium. They concluded that there appeared to

be no particular advantage in using the Bulgarian root in preference to the English, nor was there any appreciable difference between belladonna in the form of the decoction or as the standard B. P.

tincture. In 4 cases preparations of stramonium were more or equally as effective as preparations of belladonna. In 1 case belladonna seemed to be better than stramonium.

SURGERY OF THE SYMPATHETIC SYSTEM

By John C. McNerney, M.D.

Hyperhidrosis

White¹⁷⁷ suggests sympathetic denervation of the arm and leg as a safe cure for hyperhidrosis Warm and dry upper extremities may be obtained by paravertebral alcohol injection of the first and second thoracic ganglia, but alcohol may give incomplete results and at times causes intercostal neuritis Consequently, surgical denervation is considered the better procedure. It may be carried out bilaterally. Care should be exercised to avoid the ocular fibers to prevent Horner's syndrome. The highest portion of the lumbar chain in the male should likewise be left intact in order to preserve power of ejaculation

Angina Pectoris

Patients on whom surgical procedures for the relief of attacks of angina pectoris are to be performed should be selected on the basis of (1) the amount of cardiac disease present and (2) continued intense pain Although surgery offers permanent relief to those who do not respond to medical treatment, left paravertebral T2-T4 novocain-alcohol injection is safer in old men with recent coronary thrombosis, patients with rapidly progressive heart disease secondary to syphilitic aortitis, and in young individuals with active rheumatic fever and aortic regurgitation. Excellent results may be obtained in over two-thirds of these patients by injection.

Raney¹⁷⁸ describes a preganglionic unilateral section of the rami communicantes from the intercostal nerves To-T₅ and section of the sympathetic chain between the fifth and sixth dorsal gan-This procedure replaces former sections of postganglionic or afferent fibers or both Total permanent relief from attacks result notwithstanding the lack of complete interruption of the efferent pathways by bilateral section. The warning signal is not removed as in palliative afferent pathway interruption. Finally, Horner's syndrome is not produced. The surgical procedure appears to confirm recent experimental work. 179

Paroxysmal Tachycardia

The disturbance in cardiac rhythm in paroxysmal tachycardia generally arises outside the sino-auricular node in a heart free from organic disease In spite of the fact that the condition is due to an intrinsic abnormality in the pacemaking mechanism, the irritability of the heart is increased by extrinsic cardiac nerves and may be controlled by sympathetic intervention Leibovici, Dinkin and Wester¹⁸⁰ report a severe form of postoperative paroxysmal tachycardia promptly and permanently relieved by injecting 20 cc. of a 1 200 solution of procaine hydrochloride into the left stellate ganglion Horner's syndrome will confirm blockage.

It is no longer disputed that the sympathetic system likewise plays a part in sinus tachycardia. Interventions on the right stellate ganglion are effective in this condition. Because immediate permanent relief is often encountered in both paroxysmal and sinus tachycardia following injection, preliminary novocaine infiltration of the respective ganglia should always be done. In refractory cases this may be followed by alcohol injection or stellectomy.

Bronchial Asthma

Although White in 1935 in summarizing the work that had been done on bronchial asthma felt in the face of the inconsistent results that followed radical resections of both the sympathetic and vagal pulmonary ramı that it did not seem possible to recommend sympathectomy for the treatment of this condition, Leriche and Fontaine¹⁸¹ emphasize the satisfactory results (55 per cent) of bilateral stellectomy in intractable forms of bronchial asthma Preliminary infiltrations of the ganglia are of value in attenuating the development of asthmatic crises and helpful in selecting cases as patients who have a favorable response to infiltration usually have a favorable response to stellectomy.

Vesical Atony, Spasm and Pain

The diagnosis of vesical atony, the urinary tract analogue to congenital megacolon, is made by clinical, neurologic, and cystoscopic examination Huggins, Walker and Noonan¹⁸² report improvement in over two-thirds of their patients following presacral neuroctomy or resection of the superior hypogastric plexus for this condition. The proper selection of cases for operation is essential. Sympathectomy will not prove beneficial when disease has produced appreciable injury to the pelvic

nerve or sphincter with true incontinence and in tabes dorsalis.

Hypogastric (presacral) section alone provides adequate relief from bladder spasm but does not render the bladder insensitive to pain. Nesbit and McLellan¹⁸³ believe that sympathectomy for the relief of vesical pain should be resorted to in only those patients in whom pain is demonstrated to result from spasm. The 1 constant preoperative feature in these patients is spasm, while relief of spasm and ease of urination is the 1 constant postoperative feature.

Because presacral neurectomy does not relieve bladder pain of other than spasm origin, Schroeder and Cumming¹⁸⁴ suggest the additional procedure of exeresis of the lateral sympathetic chains. This more radical intervention may be followed if necessary by the postoperative injection of intrathecal (subarachnoid) alcohol to disrupt the parasympathetic and somatic pain fibers which are for the most part left intact. Care should be used to control the subarachnoid alcohol dispersion as intrathecal injection of alcohol, although simple, is not without danger. 185 Cordotomy may be occasionally resorted to for the relief of vesical pain resulting from advanced malignancy.

Dysmenorrhea

Resection of the superior hypogastric plexus reduces uterine spasm and vasoconstriction. The success of the procedure depends upon the proper selection of patients for operation. It is obvious that all pelvic pathology should be corrected, and as Meigs¹⁸⁶ pointed out, the pain in patients with primary dysmenorrhea should be referred to the region of the anus and coccyx

Untoward results, concerning which it is wiser to warn the patient, are

probable changes in menstrual habits and lack of successful orgasm during intercourse. Backache is not always relieved. There are no serious changes in bowel or bladder habits. Pregnancy is not interfered with.

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PATHOLOGY, CLINICAL

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THE EFFECT OF REFRIGERA-TION ON MALIGNANCY

During the course of investigations on body surface temperatures⁷ it was noted, that the temperature normally found in the mouth and that normally found in the extremities might vary within so marked a range as from 12 to 22 degrees. The same studies also showed that whereas the temperature of the segments of the trunk were fairly uniform, that of the segment in which the breast lies was, on the contrary, extremely variable, showing an increase of from 0.5 to 2 degrees over that of the segments lying 2 inches on either side

Now the breast is generally recognized as a frequent site of malignancy while tumors of the extremities (hands and feet) have been shown to be definitely infrequent. Recent surveys, those of Coley and Higinbotham, Mason, and Pack and Adair have emphasized this peculiarity of distribution as regards primary tumors, and Geschickter and Copeland have discussed it with relation to the occurrence of metastases in these regions

These facts, coupled with the observations recorded by Fay and Henny gave rise to an interesting speculation, was it possible that the frequency of cancer in the breast, a region in which temperature levels were relatively high, and the infrequency of malignancy in the extremities below the hands and knees, where temperature levels were relatively low, was in any way related to these temperature variations? And, as a corollary, if so, what effect could be expected from the application of low but not lethal temperatures to malignant growths?

Obviously, if any effect were probable it would most likely, if not inevitably, be an expression of the effect of low temperature upon cellular growth and reproduction But before any such effect could be consistently elicited and particularly, before it could be consistently controlled and studied, it was obviously necessary to ascertain first what constituted the critical temperature level for normal cellular growth.

Experiments by Huggins and Noonan⁵ upon the relation of changes in temperature to changes in the bone marrow in rats had already suggested that the critical level for normal embryonal cell growth was 95° F. (35° C.)

To determine whether this was a broad biologic principle, Smith⁶ studied an extensive series of chick embryos subjected to varied temperatures. These studied were significant in 2 respects: First, not only was it clearly shown that the "critical" temperature level for the normal growth pattern in chicks actually was 95° F (35° C), but also that levels between 95 and 90° F. (35 and 322° C) maintained for 48 to 72 hours, when applied at the beginning of incubation regularly resulted in deformities And, second, if cell differentiation had been established by incubation at normal temperature levels for 48 to 72 hours, then subsequent exposures to "subcritical" levels (below 95° F) even for 48 to 96 hours produced only occasional changes in the normal growth pattern

These experiments were quite different, both in method and results, from any heretofore conducted in which neoplastic and normal tissues were subjected to freezing (CO₂, liquid air, etc.) without significant injury and seemed,

perhaps, more particularly applicable to the study of cancer as a clinical problem For biopsy specimens from tumors locally treated by reduced temperatures consistently showed regressive and degenerative changes, even to a degree significant of actual stoppage and even retrogression of growth.

While these changes were, as regards nuclear destruction and cytoplasmic degeneration, quite comparable to those seen after adequate radiation, there was 1 very striking difference of great potential significance; whereas effective irradiation in adequate dosage destroys neoplastic and normal tissue alike, including the smaller blood vessels so that repair results in a dense avascular cicatrix, the effect of low temperature seems to be restricted to abnormal tissue and even when maintained for long periods, does not damage the skin or supportive tissues Repair, therefore, takes place as a normal regenerative process without the formation of true cicatricial tissue

Even before the completion of the experiments just noted Fay and Henny' had reported upon the effect, as studied in repeated biopsies, of localized refrigeration applied to a carcinomatous growth in the human being. These effects were (a) A cessation of pain, (b) definite avascularization of the carcinomatous area with shrinkage of a fungoid mass; and, (c) definite degeneration of the tumor cells locally with eventual initiation of fibrous tissue repair.

Based upon these clinical and experimental findings, speculation now advanced a step further. In view of the effect of the local application of cold to cancerous tissue, was it possible, by maintaining the entire body at a "subcritical" temperature level (85 to 90° F. or 29.5 to 32.2° C.) to produce similar regressive cell changes in metastatic foci?

With the full consent and co-operation of patients classified as hopeless and inoperable and willing to grasp at any straw in the endeavor to escape from agonizing pain, a method of producing an artificially induced "hibernation" in the human being was devised and applied by Smith and Fay,8 with results not only of extraordinary interest in themselves, but of extraordinary significance in that they open up, not only a new avenue of approach to the clinical and experimental study of cancer, but also a new field in the study of human physiology.

As so far reported (December, 1938, to October, 1939) a total of 33 patients have been subjected to 75 such periods of "hibernation," all being hopeless, terminal cases of cancer, chiefly seeking relief from pain. All had received the limit of surgical and irradiation treatment and all were in poor general physical condition.

The effect of *local* refrigeration as a therapeutic measure has been reported upon in 38 cases by Smith and Fays in which in addition, artificial "hibernation" was induced

The most striking clinical effect has been a prompt reduction in pain amounting, in most instances, to complete relief of local pain

Of particular interest are the effects seen in the local neoplastic lesions as shown by gross observation and also by the study of repeated biopsies

These are: (1) A regular measurable and rapid decrease in the gross size of the lesion, seen within 24 to 48 hours and amounting, in some cases, to as much as 50 per cent

(2) A definite retardation in the rate of growth In at least 2 cases (both relatively young, in their thirties, and both cancer of the breast with extensive metastases) there has been a complete

disappearance of the local lesion with marked retrogression of the metastases.

Results such as these naturally lead in the minds of the laity to the hope that, at long last, the hoped for "cure" for cancer has been achieved. Smith and Fay, however, strongly emphasize that this method is not a "cure" but a therapeutic measure particularly applicable to the relief of constant and intolerable pain in the hopeless, inoperable case While its practical clinical value and possibilities must necessarily depend upon numerous prolonged and extensive studies, they particularly emphasize and plead for the essential and vital importance of restricting attempts to apply it to circumstances under which it can be utilized with clear understanding and efficient control. Less than this must lead inevitably to disaster. It must be recognized that artificial "hibernation" in the study of cancer is as yet—and will remain for some time—an entirely and strictly experimental project to be relegated absolutely to the skilled and experienced investigator

Repeated biopsies taken at regular intervals have shown a rather regular sequence of events characterized as "almost inevitable."

As already noted, there is, first, a measurable decrease in the size of the local lesion which, upon microscopical examination, is seen to be due largely to a decrease in the blood supply. This may be logically interpreted as an ischemic reaction to persistent cold.

The next microscopically visible change is in the cells which show variable staining reactions, perhaps and most probably as a consequence of madequate nutrition following the decrease in the blood supply. Then, after a few days, microscopy shows evident degenerative changes varying from minimal variations in staining reaction to frank necrosis and complete

disintegration. Of definite importance and very suggestive significance is concomitant evidence of decrease in growth energy as shown by a reduction in the number of mitotic figures as well as by a decrease in the degree of anaplasia characteristic of rapidly proliferating malignant tumors.

The final stage is that of actual liquefaction and absorption with disappearance of necrotic tumor tissue.

Obviously, not all of these changes occur in all of the tumor tissue to an equal degree. But they do occur with sufficient constancy and in sufficient degree to indicate that the procedure constitutes a significant contribution to cancer research and one of potential value and importance.

Equally important is the fact that these investigations have opened up an entirely new field in the study of human physiology.

While it has long been common knowledge that periods of hibernation characterized by a slowing of normal metabolic phenomena almost to the point of complete cessation were normal events in certain species of plants and animals, it had long been believed that such periods were impossible in the human being because any prolonged exposure to temperatures sufficient to bring about hibernation (85 to 90° F. or 29 5 to 32.2° C) were accepted as incompatible with life in the human being. These studies have shown that life can be sustained under exposure to temperatures in the eighties for as long as 5 to 8 days

It will be of great interest to study the effects of this induced decrease in the metabolic rate and preliminary studies have been reported by Smith and Fay⁹ on various aspects

Based upon observations made upon 33 cases exposed to temperatures of from 74 to 90° F (23 3 to 322° ())

for periods of 5 to 8 days, they record the following:

Basal Metabolism-Because of the variation in the respiratory rate previously reported6 which in some cases showed but little change while in others it dropped to 10 or 12 and in still others rose to 28 or 30, basal metabolic readings by the usual indirect methods have been unsatisfactory and of dubious reliability. However, from 51 such determinations the impression has been gained that there is an actual reduction in the basal metabolic rate varying from as little as —6 to as much as —25 As already said, however, it is questionable whether these readings represent the actual reduction present, accurate measurement of which will probably require direct calorimetry

Blood—In view of the observations of Huggins and Noonan⁵ on the bone marrow changes occurring in white rats exposed to low temperatures; together with the fact that the precursors of the fully matured cells of the peripheral circulation might well be regarded as "embryonal" in character and, as such, for this reason comparably as vulnerable as the "embryonal" cells of neoplastic origin, the possibility that anemia might result from prolonged exposure to critical and subcritical temperatures was evident

In the earlier series of cases, while there was no striking fall in the red cell count, there was a tendency for the hemoglobin to fall slightly, this drop in one case being from 10.5 to 7 Gm. It would appear that anemia is a possible complication in refrigeration therapy, not usually apparent in the first or even second period of generalized refrigeration, but more apt to appear on further exposures.

It is somewhat difficult to evaluate accurately the cytological studies thus

far made of the blood of these patients because of the difficulties inherent in several factors dependent upon the disease they present. Among these are the anemia consequent upon the cachexia common to advanced cases of malignancy; and alterations in blood volume, rate of blood flow and blood pressure, all of which greatly increase the difficulties of estimating the statistical significance of the observations recorded.

In the case of the leukocytes, however, the variations are definite and striking. A definite and sometimes marked leukocytosis—up to 50,000—frequently occurs after 24 to 48 hours of refrigeration, the average level being 15 to 20,000. The differential count shows but little change, the polymorphonuclears averaging 60 to 75 per cent in the majority of cases, although in one case during the course of 4 exposures in which the total white cell count ranged from 14,850 to 44,800, the polymorphonuclear percentage reached 93

The explanation for these changes is not yet apparent

Circulation Time—Preliminary studies suggest that the circulation rate is nearly doubled in the peripheral vessels, possibly because of an actual increase in the blood viscosity

Blood Chemistry—These observations are as yet not numerous but those so far made have shown no evidence of nitrogen retention, indeed, not infrequently there has been a slight drop from the average figure and, where fluid balance has been maintained, the drop in the blood urea has been pronounced with readings as low as 4 mg. with an average of 10 mg. per cent.

Blood sugar also has shown a reduction to an average of 80 to 90 mg. per cent in 54 determinations. In the majority of cases the blood sugar ranged from 110 to 120 mg. per cent.

In general, when fluid balance is maintained, there have been no significant variations in the blood chemistry

Renal Function—As suggested by the lack of any evidence of nitrogenous retention in the blood, renal function has shown no evidence of impairment when care is taken to maintain fluid balance, and, in cases subsequently studied at autopsy, there has been no evidence of any damage to tubules or glomeruli as a result of the prolonged exposure to cold.

It is apparent, of course, that these are but fragmentary and incomplete studies but, as far as they go, they are of interest.

PRESENT STATUS OF PRESERVED BLOOD

During recent years the "blood bank" 10 has been received with considerable enthusiasm and has achieved widespread popularity as a source of supply for transfusions

Accumulating experience, however, has definitely modified some of the original concepts upon which this procedure is based and the studies of various investigators have shed much light upon the effect upon blood of various methods of preservation and storage. As these studies are of practical value and importance they are here summarized and discussed

Methods of Storage—It is universally accepted that refrigeration must be at a temperature of from 39 to 43° F (4 to 6° C), but it has not always been recognized that, to prevent wastage, this level must be maintained with satisfactory and dependable constancy. Attention has been called to this by Diggs and Keith¹¹ who recommend the following precautions

1 Periodical inspection at 3-hour intervals by a member of the hospital engineering staff who is responsible for the upkeep of the motor.

- 2. Installation of warning signal lights on the refrigerator which signal any drop of temperature below 32° F. (0° C.) or any rise above 43° F. (6° C).
- 3. Placing the refrigerator on an electric circuit separate from all other electric appliances.
- 4 Installation on the refrigerator of a recording thermometer so that not only is the temperature visualized at all times but the duration and degree of any failure is recorded

Preservative — Widely used is the method of Cook County Hospital¹² consisting of the addition of sterile 2.5 per cent sodium citrate in the proportion of 14 cc. to each 100 cc. of blood producing a 0.35 per cent concentration of citrate

While sodium citrate is the most popular anticoagulant in the United States, various other and more complex solutions are also used in Europe and Canada

Thus, Goodall¹³ who introduced placental blood as a source of supply for transfusion, uses that originally recommended by the Moscow Hematological Institute

Sodium chloride	7.0	Gm
Sodium citrate .	50	Gm
Potassium chloride	0.2	Gm
Magnesium sulfate	0 04	Gm
Bi-distilled water	. 1000	cc

This preparation is now commercially available in ampoules under the name of "citro-seroid"

Gwynn and Alsever¹⁴ use the following formula:

Dextrose	20 0 Gm
Sodium citrate .	50 Gm
Sodium chloride	. 46 Gm
Distilled water	.1000 cc.

This is prepared as 2 solutions, 1 containing the dextrose, the other the salt and citrate and 50 cc of each placed in the collection flask just prior to the collection of blood

Duration of Storage—In the early days of blood banking it was believed that preserved blood could be successfully stored for as long as 3 weeks. Cumulative experience has resulted in a somewhat drastic revision of this concept and the consensus now places an extreme limit of 5 to 7 days for satisfactory preservation. As will later be discussed, the underlying purpose for which preserved blood is to be used is a very important factor in determining the duration of effective storage.

Quite obviously, hemolysis furnishes gross evidence of blood deterioration. Gwynn and Alsever report that, with the Moscow preservative solution, hemolysis is visible after 3 days and marked after 10 days. Contrary to the conclusions of many other workers, they believe that blood preserved with their formula will remain in a satisfactory state for use in transfusion for as long as 8 to 10 weeks. This they believe due to the presence of dextrose in their solution which, they recall, was suggested by Belenkiy 15 in 1936.

Hemolysis is, of course, an indication of increased red cell fragility and many observers have demonstrated that red cell fragility increases pari passu with the duration of storage. As a consequence, it is rather generally agreed that undue agitation (shaking) of stored blood should be avoided in order to delay hemolysis in massive degree.

The degree to which hemolysis in transfused blood may be related to posttransfusion reactions is a matter concerning which there is some difference of opinion

On the one hand, it is believed by some investigators^{16, 17, 18} that hemolytic transfusion reactions result from the blockage of renal tubules by hemoglobin precipitated in acid urine. On the other hand, Bayliss¹⁹ has shown

that hemoglobin may pass out in the urine without harmful effect. Belke. Henry and Rosenstein²⁰ state that though jaundice and hemoglobinuria are somewhat more frequent after the transfusion of stored blood than after fresh blood, an observation in conformity with that reported by Fox,21 they also comment that such occurrences are not in most instances accompanied by other evidences of true hemolytic reactions such as chills, fever and impairment of renal function. They believe, therefore, that true hemolytic transfusion reactions depend upon something more than simple intravascular hemolysis.

In any event, there is a definitely growing opinion and rather general agreement that the period of safe and efficient storage of blood for transfusion is much less than was originally thought and probably may be stated as averaging 5 days with a maximum limit of 1 week. From this it follows that blood banks can only be conducted efficiently and without excessive wastage when the number of transfusions is sufficient (100 per month or more) to allow of a rapid turnover which would relegate the blood bank to the relatively large and active institution

Cellular and Other Changes In Stored Blood—Plasma Potassium—Scudder, Drew, Corcoran and Bull,²² report upon the repartition of potassium in cells and plasma and corroborate the observation by Dulière²³ that there is a progressive increase in the serum potassium of stored blood.

The importance of this observation lies in the fact that in potassium poisoning in greater or lesser degree may lie the explanation of posttransfusion jaundice and, perhaps, of the occasional inexplicable posttransfusion fatality The observations of these workers were extensive and carefully controlled and their results may be thus summarized:

In preserved blood stored under aseptic and bacteriostatic conditions there is a daily, progressive increase in the plasma potassium reaching even as high as a 1000 per cent over the normal. This increase results from a progressive diffusion of potassium from the cells to the plasma which begins with the withdrawal of the blood, is at first rapid and later slows, though still continues, and is not prevented by any of the preserving solutions in common use.

It was also shown that this diffusion of potassium was, in some degree, influenced by the shape of the container in which the blood was stored, being directly related to the extent of the interface area between the cells and the supernatant plasma, and hence less in tubular than in wide-bottomed containers; that the rate of diffusion was greatly increased by shaking; and that, as there was no parallel between the rate of hemolysis and the diffusion of potassium, the degree of hemolysis cannot serve as an index of the plasma potassium in preserved blood It is emphasized by these observers that a high degree of potassium diffusion may be present in the complete absence of visible evidence of hemolysis.

From these studies, the results of which are in conformity with others, it follows that blood stored for periods sufficiently long to permit diffusion of potassium in marked degree should not be used for transfusion in conditions associated with hyperpotassemia. Among such conditions are severe burns, intestinal obstruction, intestinal fistula, the dehydration of cholera, renal and hepatic insufficiency, typhoid fever, pneumonia, influenza, and certain disorders of the

ductless glands associated with disturbances of salt metabolism (parathyroid tetany and the collapse state of addisonian crises).

Likewise in hemorrhage and shock, in which there is experimental evidence of potassium disturbance, stored blood must be used with some degree of caution, although many reports have shown that when the storage period is not prolonged and the transfusion technic acceptable the incidence of reactions in such cases has been low.

Cytological Changes-There is, perhaps, a fairly common tendency to regard the function of transfused blood as mainly concerned with a restoration of volume and as a means for the replacement of erythrocyte loss. But it must also be borne in mind that blood is a complex tissue containing leukocytes, blood platelets, varied chemical substances such as prothrombin, complement and the like. And, because the blood is the important avenue of transport for oxygen and carbon dioxide, the importance of knowing to what degree these blood components and properties are altered by preservation and storage of blood becomes readily apparent. These phases have not been overlooked by various observers whose work will now be discussed.

Erythrocytes — Observations concerned with the occurrence, rate and degree of hemolysis—which is, of course, related to red cell fragility—have been discussed above and need not be repeated.

While, as might be expected, increasing red cell fragility and increasing evidence of hemolysis go hand in hand, it should be noted that evidence of changes in the red cells (swelling and dehemoglobinization) are demonstrable in citrated blood as early as 48 hours, progressing thereafter so that at 14 days

at least 30 per cent of the erythrocytes are "blood shadows" (Kolmer).

Because of their function as oxygen transport these early and progressive changes are of definite interest.

Blood Platelets—While a complete understanding of the full function of the blood platelets has yet to be achieved, their important relation to the phenomenon of coagulation is generally recognized And as transfusion is a therapeutic measure frequently resorted to in blood dyscrasias and diseases associated with disturbance of the bleeding and coagulation time, the effect of storage upon blood platelets is of obvious interest

Belk, Henry and Rosenstein²⁰ report a marked drop in 24 hours, a further marked drop at 48 hours and then a slow fall up to 20 days which marked the limit of their observations.

Kolmer²⁴ records immediate clumping and evidence of platelet disintegration in 24 hours resulting in a scarcity of platelets after 48 hours, and after 5 days the presence of only blue chromatin masses

Leukocytes—One of the reasons for the use of transfusion in the treatment of acute infections, though, perhaps, of relatively minor importance, is that through transfusion a new force of phagocytes may be brought to the battle

The observations reported by Kolmer²⁴ on the effect of sodium citrate on the opsono-phagocytic activity of pre-blood are hence of interest and importance

Tests conducted against Staph, aurcus, B. coli and a beta hemolytic streptococcus (Group A) begun at once after collection of the blood and continued at regular intervals up to 21 days, the blood being stored at 39 to 43° F. (4 to 6° C.), showed a definite reduc-

tion of the phagocytic activity of the neutrophils within 72 hours, a marked loss after 5 days with a complete disappearance after 7 days. While, as Kolmer comments, this may in some degree be related to a deterioration of normal opsonins, it was in greater measure consequent upon autolytic and degenerative changes in the leukocytes.

It is appreciated, of course, that the bacteriostatic and bactericidal properties of human blood vary within indeterminate limits in the individual, and also that they are the expression of complex and correlated interaction involving various components and properties of the blood, among which, in addition to leukocytic phagocytoses, may be mentioned opsonins, bacteriolysins, nonspecific leukins and plakins and—not least—complement

While any direct or accurate measurement of many of these is a matter of some difficulty, Kolmer reports that the blood of 3 donors seeded with the organisms used for the opsonic determinations, showed a definite loss of bacteriostatic and bactericidal properties for one or more of the organisms as an aftermath of storage.

Complement — While the bacteriostatic ability of the blood is in some measure dependent upon the bactericidins effective without the presence of complement (nonspecific leukins and plakins), the most important factors concerned with the normal bactericidal activity of the blood are bacteriolysins for the effective action of which complement is essential

While some workers have reported that sodium citrate in concentrations of 0.25 to 0.35 per cent is destructive for human complement, the investigations of Kolmer²⁴ demonstrate that while there is some reduction, in terms of hemolytic activity, in the complement of citrated

human blood stored at 39 to 43° F. (4 to 6° C.) this loss in minimal and, in general, complement is well preserved up to 2 to 3 weeks, after which some deterioration sets in.

From this general and admittedly not comprehensive review it is possible to draw certain general conclusions.

First, it may be said, that in view of the investigations discussed, the period of efficient storage of preserved blood may be stated in general as from 5 to 7 days.

Second, a "blood bank" can only be efficiently conducted when the number of transfusions is conducive to a rapid turnover, from which, as a corollary, it follows that "blood banks" properly belong to large and active institutions and cannot be efficiently conducted, nor with suitable economy of the blood collected for storage in the smaller and less active hospital

It is theoretically ideal to think of a blood "bank" as an inexhaustible supply of blood of any type desired. But the ideal is seldom reached in practice. And there is some reason to believe that the fact that there is a blood bank has led to an increase in the use of transfusion without thorough consideration of the circumstances essential to the valid use of this procedure as a therapeutic measure

The final criterion which should govern the selection of the type of blood used for transfusion (fresh or preserved) should be the indication for the transfusion itself

Contraindications to Preserved Blood—While preserved blood may be used to good effect in perhaps the majority of conditions in which transfusions are indicated or rather generally used, there are others in which there is a growing concensus that it should not be used

Among the conditions in which preserved blood is considered to be unsuitable and inefficient as compared to fresh, whole blood may be mentioned blood dyscrasias, anemias (Kolmer), agranulocytic angina (malignant neutropenia), purpura hemorrhagica, hemophilia, vitamin K deficiency and, perhaps, all hemorrhagic diseases (Belk, Henry and Rosenstein).

Certainly, if preserved blood is used under these conditions it should not be more than 24 to 72 hours old

Perhaps the 1 condition in which fresh blood transfusion is definitely and always to be preferred is when transfusion is used as a therapeutic measure in acute infections.

Transfusion in the presence of acute infections is no longer generally regarded as solely a measure to combat the frequently associated secondary anemia. It is now appreciated that transfusion serves as a source of renewal of specific and nonspecific immune substances as well as increasing the available number of efficient phagocytes being true, in the light of the changes and alterations shown to occur in preserved blood, it can safely be said that whole blood is definitely to be preferred and that if preserved blood must be used, it should not have been stored longer than 48 hours

Blood Donor Registry—While "blood banks" should theoretically be most useful to the small hospital where donors are not always readily available, it has several times been commented that this is just the situation in which they may well be the most inefficient and wasteful

For this reason Pons²⁵ has called attention to the value of the blood donor registry as a substitute for the blood bank

In all too many instances the transfusion problem is apt to be complicated in the small hospital by factors not as frequently operative in the larger institution.

The first of these is that the transfusion appears as a sudden and acute emergency when, as a matter of fact, the possibility of this eventuality could have been foreseen and anticipated in ample time to permit unhurried preparation for it

As a rule, the majority of transfusions do not represent an attempt to meet a real and sudden emergency in the shape of massive and unexpected blood loss. In many instances they represent an attempt to "do something" in a hopeless case more for the satisfaction of excited relatives than for any real benefit which may be rationally expected. In others, such as in blood dyscrasias, acute infections, and so on, it is undoubtedly true that there is often little reason to doubt but that the indications and necessity for transfusion could be foreseen and foretold sufficiently in advance to allow for a quiet and orderly performance of all the procedures preliminary to the actual transfusion and, indeed, for the actual transfusion itself as a routine rather than a "stat" emergency measure.

In any event, Pons calls attention to the fact that not only is a blood donor registry an efficient substitute for the blood bank in the smaller hospital, but the establishment of such a registry is relatively easy and simple. The essential feature of the donor registry proposed by Pons is that it is not a registry of professional donors whose services are to be purchased, but a registry of volunteer donors whose services are freely given

In registering such donors, the first sources of which are the friends and rela-

tives of the patient, it is explained that the registry is intended to fill the place of the blood bank in that it will furnish a constant and readily available source of blood as and when needed; that when the volunteer donors prove not to be suited to the particular patient in question delay will be eliminated by calling on a registered donor who *is* suitable as they, in turn, may likewise be called.

In order to maintain the co-operative principle, when a donor cannot readily be obtained from relatives and friends, they are given a list of donors of the type needed in order that they may select and approach one. In this way the burden of obtaining a donor rests upon the patient's relatives or friends. Pons comments that it is easy to develop community interest in the project and that any organized public campaign is unnecessary. As an illustration, he reports that during 1938, 3200 donors were typed at 2 hospitals having a combined capacity of 375 beds

For the efficient operation of such a registry proper organization is essential As carried out by Pons, the following plan is used

It is essential that the files of donors be in charge of a clerk trained to understand the fundamentals of blood grouping and cross-matching, but not necessary that this clerk be a technician as it is preferable that the files be kept in the main hospital office

The name, address, blood type, and telephone number of the donor are recorded in the laboratory when the typing is done and these data passed on to the registry files in the main office.

No reports are made nor requests honored by telephone; all requests for donors and all arrangements for typing, cross-matching and the transfusion itself are made through and by the transfusion clerk.

When a transfusion is decided upon, the following request is sent to the transfusion clerk:

TRANSFUSION CLERK Date

I have notified the relatives/friends of (Ward Room) that we plan to give him/her One (1), Several () transfusions Please make the necessary arrangements.

Signed

The transfusion clerk then transmits the request to the laboratory, having arranged with the relatives and/or friends to report for examination. Should they not prove suitable, they are given a list from the registry of donors of suitable type whom they are to approach.

The following forms are used:

REQUESTS FOR TYPING AND CROSS TYPING Patient's name

Room Blood type

Ward

Donor Type

LABORATORY TRANSFUSION REPORT

Date

Room

Ward Patient's name Blood type Donor's name Blood type Address Tel No Cross agglutination is

Kline test 1s

Expected date of transfusion

Transfusion Reactions—No discussion of blood transfusion can be considered complete without some consideration of transfusion reactions.

While there is no reason to believe that the incidence of posttransfusion reactions is necessarily any greater, if at all, than after transfusions of whole blood, it must be admitted that statistics concerning this are somewhat difficult to interpret, principally because there appears to be no uniform agreement on what constitutes a reaction

If, as is done by some, a rise in temperature of more than 1 degree is regarded as a reaction, the incidence will naturally be higher than when only severe and obvious manifestations are recorded, such as chills.

There is little reason to doubt, however, Plummer's²⁶ statement that 50 per cent of patients "are at least mildly inconvenienced."

Fell²⁷ in a careful survey of 500 transfusions reports 48 reactions, an incidence of 11.6 per cent and there is little reason to doubt that in the relatively small institution the incidence of reactions may be even greater

In view of the circumstances under which transfusions are given, it is apparent that all transfusion reactions, however mild, are undesirable and, when more than mild, may readily be harmful if not actually dangerous. That they are preventable is shown by Lewisohn and Rosenthal²⁸ using citrated blood with 1 per cent of reactions; and the more recent report by Patton²⁹ using citrated and refrigerated blood with an incidence of 09 per cent of reactions in 920 transfusions.

Prevention of transfusion reactions, whether with whole or stored blood, depends largely primarily upon an understanding of their nature and cause. Bonnin³⁰ has recently reviewed the subject in extenso and his paper will largely be drawn upon for the comments to follow

Bonnin groups the complications of blood transfusion under 5 main headings (1) Transmission of disease, (2) hemolytic reactions, (3) allergic reactions; (4) pyrexial reactions; (5) reactions due to faulty technic

It is appreciated, of course, that these groupings are in no way mutually exclusive and that it is possible for any or all in any combination to play a part in a single transfusion reaction. Indeed,

this possibility may in some measure account for the difficulty experienced in attempting to classify transfusion reactions on the basis of symptomatology.

Transmission of Disease—The particular possibility here envisaged is the transmission of syphilis and it must be admitted that, as yet, there is no absolutely certain possibility of avoiding this risk.

While it is common knowledge that negative serology is a *sine qua non* in the determination of the suitability of a donor, even this precaution has its pit-falls and may lead to a fallacious sense of security.

In the first place, it must be appreciated that negative complement fixation reactions periodically performed cannot be accepted as indisputable nor irrefutable evidence of freedom from syphilis in the professional donor. For a negative complement fixation reaction on a given date applies only to the *status quo* and carries no guarantee for the future

Moreover, as is well recognized by serologists and syphilographers, serologic positivity is not synchronous with the acquisition of syphilis but appears only after the disease has been in action long enough to provoke sufficient tissue activity to lead to the production of reagin in *detectable* amounts. Hence, a donor with a newly evident chancre less than 12 to 21 days old may have a negative reaction.

For this reason, many serologists are in agreement with Rein, Wise and Cukerbaum³¹ in believing that every donor should be subjected to some serologic test—such as one of the precipitation reactions—immediately prior to the transfusion

In the author's laboratory, this has been the practice for many years Before a donor can be reported as suitable, the following criteria must apply: (1) The

blood type must be the same as that of the recipient; (2) the cross-matching must show no incompatibility; and (3) the Kline test must be clearly and cleanly negative. In addition, knowing that in a small proportion of cases, the complement fixation test may be negative while the precipitation test is positive, and vice versa, a complement fixation test is also done. When the transfusion is to be done at once, the donor is passed on a negative Kline test. Where time permits, the results of both tests are awaited

While it seems beyond belief, it is still true that, in some places, donors are used without any attempt to determine their serologic status. This, of course, is entirely and absolutely indefensible and should neither be permitted nor condoned.

Oddly enough, it seems to be quite frequently overlooked that while the function of the laboratory properly includes the determination of blood type, blood compatibility and serologic status, it does not include any responsibility for physical examination. It is the duty of the clinician who is responsible for the actual transfusion to be responsible also for the absence of physical evidence of syphilis or any other communicable disease. Even a cursory examination may discover the concealed or unrecognized recent chancer which has not yet produced a positive serology.

Bonnin calls attention to the value, also, of an inquiry into the history (possible exposure, etc.) suggesting that it is hardly likely that a donor willing to give blood would want to run the risk of giving syphilis with it.

It will not be possible here to discuss the transmission of disease in general by transfusion, though the possibility of transmitting malaria in localities where the disease is endemic should be mentioned, and it is not amiss to emphasize that, as shown by reported cases, such transmission may occur when the disease has long been latent and practically asymptomatic in the donor.

Hemolytic Reactions — The commonest causes of hemolytic reactions are technical error, incorrect grouping, failure to substantiate the blood grouping by a direct compatibility test, failure to specify the classification in use (Moss or Jansky; not necessary with international), and blind reliance upon the "universal donor" and "universal recipient."

The author has long believed and long preached that the essential prerequisite for the selection of a donor is that he shall be the same type as the recipient!

Incidentally, it should be emphasized that the commonest cause of errors in blood typing is the use of *low* titer typing serum.

Many reports are extant on the occurrence of reactions, sometimes severe even to fatality, consequent upon the use of a donor who had previously been used without any reaction. While some of these reactions have been apparently allergic in origin—for which reason, many authors believe in the use of fasting donors—others have been hemolytic in character. There is some question whether these are the result of the development of specific hemolysms, but because of the possibility of their occurrence Bonnin believes that no donor should ever be used twice for the same patient. In the author's experience "same donor reactions" have not been frequently seen

Fantus, Seed and Schirmer³² call attention to the fact that hemolytic reactions are apt to occur when the patient is already suffering from a hemolytic disease. In such cases they recommend that transfusions be small and repeated rather than massive, and preceded by alkalinization of the urine to prevent the deposit of acid hematin in the kidneys

Allergic Reactions—These are usually mild, urticarial in nature, and relatively infrequent. They may be symptomatically controlled by adrenalin and prevented by using the "fasting donor." Fantus¹² warns of the danger of using as a donor for a patient who has recently received therapeutic serum an individual allergic to that serum and this possibility should be borne in mind

Pyrexial Reactions — The long discussion of the probable cause of these reactions has now been stilled by appreciation that pyrexial reactions are produced by thermostabile bacterial toxins which are likely to be present in the first few hundred centimeters of water collected from a simple still. Their elimination depends upon the use of distilled water from a baffled still which should not be too old before it is used and the thorough and meticulous cleansing of all transfusion apparatus

Some pyrexial and even hemolytic reactions may follow the careless warming of refrigerated blood prior to transfusion. It is now known that such warming is unnecessary

Reactions Due to Faulty Administration—These are much commoner than is realized and some, at least, of the reactions attributed to other causes are at times due to one or other of the faults listed below

1 Too rapid administration may produce "speed shock," delayed pulmonary edema, or even death.

All transfusions, and particularly massive transfusions, should be given slowly

2. Injection of small clots from dirty apparatus or incompletely citrated blood may theoretically be responsible for delayed pulmonary complications. For this reason a filter should always be interposed in any gravity apparatus for transfusion

Patton²⁹ lists as important in the prevention of transfusion reactions with stored blood:

- 1. Avoid heating the blood.
- 2. Avoid unnecessary agitation.
- 3 Avoid the use of harsh cleansing materials in the preparation of transfusion apparatus.
 - 4. Prompt refrigeration at 39° F. (4° C).
 - 5. Use of practical equipment
- Autoclave transfusion equipment within
 hours after the beginning of cleansing procedures.

INTERPRETATION OF THE 1 HOUR-2 DOSE DEXTROSE TOLERANCE TEST

(Exton-Rose Procedure)

In 1931, Exton and Rose^{33, 34} introduced the 1 hour-2 dose dextrose tolerance test as a more delicate and reliable method for the diagnosis of diabetes by means of glucose tolerance determinations.

This method is based upon what has come to be spoken of as Allen's35 paradoxic law of dextrose utilization which may thus be summarized. The more sugar given by mouth to the normal individual, the more is utilized. There is no real limit to the normal ability to utilize dextrose and the so-called limits of tolerance in the normal individual are apparent rather than real. In the diabetic, on the contrary, the mability to handle dextrose is real and large doses of sugar administered to such individuals are not utilized and, as a result of overdosage, assimilation may be made worse rather than better

The method introduced by Exton and Rose and termed by them "the 1 hour-2 dose dextrose tolerance test" constituted a real advance in the study of diabetes, has come into wide use and is rather generally now spoken of as the Exton-Rose procedure

Although the technic is well known, for the sake of completeness it will be given here

Method — Dissolve 100 Gm of glucose in 650 cc of water The mixture.

an approximate 15 per cent solution, is flavored to taste with lemon juice and divided into 2 equal portions, each containing 50 Gm. of glucose. It should be served ice cold.

The test is carried out after an overnight fast as follows:

- 1 Collect a sample of urine and a sample of blood for sugar determination
- 2. Administer the first dose of dextrose solution, allowing 1 to 2 minutes for ingestion.
- 3 Thirty minutes later collect a second sample of blood and administer the second portion of glucose solution.
- 4. Thirty minutes later, collect a second sample of urine and a third sample of blood

Both urine samples are examined for sugar and blood sugar determinations are made on all blood specimens.

The criteria of Exton and Rose for the interpretation of the test were as follows

A. Normal Tolerance Curve:

- 1 A fasting blood sugar with normal limits
- 2 A rise not exceeding 75 mg in the 30-minute blood sample
- 3 In the 60-minute sample, the blood sugar level should be the same or less, or does not exceed that of the 30-minute sample by more than 5 mg
- 4 All urine samples should be negative to the Benedict test

B Diabetic Tolerance Curve:

- 1 A more or less steep curve of not less than 10 mg of blood sugar after the second dose of glucose
- 2 The relation of the blood and urme sugar values to the severity of the disease.

C. Renal Glycosuria Tolerance Curve:

- 1 Sugar in both urine specimens
- 2 Blood sugars which never reach the diabetic level and, in general, follow the normal tolerance curve

D. Alimentary Glycosuria Tolerance Curve:

- 1. A sugar-free urme after fasting with sugar in the final urine specimen.
- 2 Blood sugars which follow the normal curve even when the level is above normal

With increasing use of the Exton-Rose procedure, admitted generally to be superior to the methods heretofore in use, among those having extensive experience with it, the opinion began to gain ground that the criteria proposed by Exton and Rose for the interpretation of the results of the test might, perhaps, be a little too rigid.

This opinion was first expressed, perhaps, by Gould, Altshuler and Mellen,³⁶ who proposed their modification, in brief, as follows, basing the diagnosis of diabetes upon the occurrence of at least 2 of the 3 postulates following:

- 1 A fasting blood sugar of more than 120 mg per cent
- 2 A 30-minute blood sugar exceeding the fasting level by at least 50 mg.
- 3 A 60-minute blood sugar exceeding the fasting level by at least 30 mg.

For their criteria these authors claimed 100 per cent specificity and 97 per cent sensitivity for the test

Recently, Mathews, Magath and Berkson³⁷ have restudied the question and propose a still further modification of the Exton-Rose criteria.

Agreeing that the Exton-Rose procedure is based on sound phsyiologic principles, they also feel that the diagnostic criteria originally proposed are apt to lead to a relatively large number of curves which, while definitely abnormal, are yet not in conformity with the Exton-Rose criteria and hence, nondiagnostic.

They comment that whereas in the Exton-Rose criteria the 1 essential requisite for the diagnosis of diabetes is that the 60-minute blood sugar shall exceed the 30-minute level by 10 mg or more, in the criteria proposed by Gould, Altshuler and Mellen 2 out of 3 of the criteria advanced by these authors must be present. Here, again, curves occur which though abnormal are not diabetic

according to these criteria and hence also nondiagnostic.

Mathews, Magath and Berkson therefore studied 364 individuals, of whom 117 were considered normal and 247 diabetic, all subjected to careful clinical study and to the Exton-Rose procedure.

When the results of the 1 hour-2 dose test were interpreted by the Exton-Rose criteria, 96 per cent of the 247 diabetics were recognized as such. Interpreted by the criteria of Gould, Altshuler and Mellen, 77 per cent were diabetic.

In the entire series of 364, the Exton-Rose criteria yielded an agreement with the clinical diagnosis of 88 per cent and that of Gould and his associates an agreement of 73 per cent

From a consideration of the minuta developed during the course of their investigations, Mathews, Magath and Berkson present a further modification of the criteria for the diagnostic value of the Exton-Rose procedure, which, because of the careful controls in their work, and for the reasons discussed at length in their communication—which should be read by all interested in this matter—is of distinct importance and value

Their findings may be thus briefly summarized:

They believe that for the evaluation of the Exton-Rose procedure the most effective criterion is the 1 hour blood sugar value. Taking 158 mg per 100 cc as the critical level, readings at or above this are classed as presumptively diabetic and readings below as normal. With this criterion, they found a high percentage of correct diagnoses. In the series tested all individuals with readings at 60 minutes of less than 154 mg. per 100 cc were clinically normal and all those with blood sugar levels above 180 mg per 100 cc clinically diabetic

By their criterion, the nondiagnostic tests were fewer than with any other criterion used.

They comment, first, that, though a fasting blood sugar in excess of 120 mg. per 100 cc. is diagnostic of diabetes, only 21 per cent of the 247 diabetics in their series in whom the diabetes was minimal, exceeded this level. On the other hand, the fasting blood sugar never exceeded 110 mg. in their normal individuals.

Second, though a progressive elevation of the blood sugar level was demonstrable at every phase of the blood sugar time curve obtained with the Exton-Rose procedure, it was never sufficient in degree to invalidate the critical level (158 mg. per 100 cc.) they propose nor the acceptance of a fasting level above 120 mg per 100 cc. as diagnostic of diabetes

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PSYCHIATRY

Edited by Kenneth E. Appel, M.D.

MENTAL DEFICIENCY

By Robert A. Matthews, M.D.

Mongolism

Clemens E. Benda¹ compared the normal development of the skull with the development in mongolism which revealed that the growth in mongolism is delayed in length and that the failure of postnatal growth is most marked immediately after birth during the first 2 years of life. After that time the growth rate in mongolism corresponds with the normal growth rate but comes to an earlier arrest

In order to decide the question whether the delay of growth in length of the skull was due to resorption of cartilage and early ossification which would suggest hyperthyroidism, or to lack of ossification due to hypothyroidism or to a general growth disorder, due to a deficiency of growth factors, a histologic study of the skull base was carried out. Growth at the skull sutures is extremely slow and insufficient. This study adds new evidence to the author's assumption that neither hyper- nor hypothyroidism is of primary importance in mongolism. The lack of growth is thought to be due to a deficiency of more essential factors.

An x-ray study of the skull of mongoloids showed that the skull features are essentially fetal in shape and proportion, thus adding new evidence that mongolism is "not so much abnormal development" as it is arrested growth and lack of metamorphosis.²

Discussing the factors which lead to such arrest of development, Benda pointed out that various agents effective during fetal life may cause temporary arrest of growth. Shortly after birth, the diagnosis of true mongolism may render severe difficulties and one has to be careful, especially in twins.

True mongoloid deficiency represents a growth disorder with some definite histologic and gross characteristics, lack of growth in length, lack of sinus development, small diploe, splanchnomicry, sexual hypoplasia, symptoms which indicate a deficiency of hormone factors which stimulate differentiation, according to Benda Continuing, he states that these factors are probably related to the anterior lobe of the pituitary but are different from the pure "growth hormone."

Benda³ also examined microscopically the pituitary bodies of 13 supposedly mongoloid patients and 1 case of premature birth The alterations which appeared to be peculiar to mongolism consisted of an increase of eosinophilic cells and a deficiency of basophilic and chief cells, which allowed the author to believe that because the size of the pituitary is not increased and no signs of eosinophilic hyperactivity are found, the absence or deficiency of basophilic cells appears to be the most important observation The general disorder seems to be a particular pituitary deficiency of the mother during pregnancy The advanced maternal age, frequently observed in cases of mongolism, and other factors indicate that the maternal organism does not adjust itself well to a new pregnancy

Meyer and Jones⁴ found histologic changes in 10 of 15 cases of mongolism. These changes consisted mostly of widespread proliferation of the fibrous glia, which often was not accompanied by corresponding changes in the myelin and cells. They do not believe that the observations represent the pathological substrate of mongolism and point out that not enough is known about the reaction of the brain to bodily diseases, especially in infancy and childhood, and therefore it cannot be decided whether this reaction is more severe in persons with mongolism than in other defective and in normal persons.

Bixby⁵ carried out various biochemical studies in mongolism and found the blood groups to be practically the same as that of the general American population and unlike that of the Mongolian races, which is considered as opposing the hypothesis that mongoloid defect is due to a racial regression

Basal metabolic rates were minus according to the Mayo Foundation standards but usually came within normal range when the Talbot-height standards were used. These results seemed to rule out hypothyroidism as a condition of mongolism after the sixth year.

The fasting serum cholesterols of 50 mongoloid patients were found to be within normal limits and indicate that hypothyroidism is not present in mongolism, at least after the second year.

The fasting blood sugars were within the normal range in 51 cases

Ten glucose tolerance tests indicated delayed glycemic response, consistent with hypofunction of the pituitary.

Thompson⁶ has shown that the frequency of colored Mongolians is larger than was formerly supposed but is less than 2 per cent and that a little more than 1 per cent of the total number of Mongolians are colored, although there

are approximately 9 per cent colored people in the United States.

Heredity

Penrose⁷ states that in all grades of mental defect, heredity plays an approximately equal part, but the degree of dominance of the hereditary factors is different in the various grades. The defects in idiots and imbeciles are often recessively determined or are due to fresh mutation and are less obviously hereditary than those in simpletons, who, like normal persons owe their mental grade to the interaction of dominant additive factors. Environmental influence may be the only cause in comparatively rare The external circumstances are likely to be even more important in mild than in severe mental deficiency, for their effects may make the difference between certifiability and normality.

Diagnosis

Strauss⁸ considers that 2 clinical types of mental deficiency are dealt with, namely, the exogenous and the endogenous The exogenous represents any type of mental defective in whose immediate family there is no history of mental deficiency and whose case history indicates a prenatal, natal or postnatal disease or injury which appears to have damaged the brain and in which there is a strong probability that this brain defect is the cause of mental retardation. The endogenous type consists of any mental defective in whose immediate family (grandparents, parents or siblings) there occur 1 or more cases of mental defect and in whose case history there is no evidence of brain disease or injury. Those cases in which there is a possibility of a combination of both types are called mixed

Two groups of 40 children each, 1 of the exogenous type and the other the endogenous, were compared in relation to mental and corporal growth. In the endogenous cases the curve of growth in height lies equidistant between the chronological age curve and the mental age curve. In the exogenous group the curve of growth in height is nearer to the chronological age curve and farther from the mental age curve.

The rate of mental growth of the 2 types was compared by means of a series of intelligence tests extending over a mean period of approximately 8 years per child. It was found that the endogenous group showed a relatively very marked deceleration of mental growth with increasing chronological age The exogenous group showed such a deceleration but relatively much less markedly. The 2 groups differ in their response after admission to a more favorable environment such as a special residential The marked deceleration of the endogenous group is then replaced by a trend toward relative acceleration the exogenous group, the trend of mental growth is not appreciably affected by the environmental change

Jervis⁹ has studied the genetics of a recently discovered form of mental deficiency, now known as phenylpyruvic oligophrenia

Folling in 1934 reported findings of phenylpyruvic acid in the urine of 10 mentally defective children and in 6 of these the condition was present in 2 siblings. In 1935 Penrose suggested that the disease might be due to recessive genes. The present author, Jervis (1937), basing his conclusion on the study of 50 cases offered evidence for the hypothesis of a single recessive gene substitution.

The disease is characterized by an alteration of the metabolism of phenylalanine There is strong evidence indicating that this amino-acid is not oxidized by the organism. An abnormally high amount of phenylalanine, in fact, is found

in the blood. The phenylalanine is then transformed into phenylpyruvic acid mainly by the kidney, and this last acid is excreted in the urine. Clinically, the disease shows a fairly well-defined symptomatology. In the majority of cases anomalies of the motor system are demonstrable; increase of the muscle tonus. hyperactivity of the deep reflexes, knee and ankle clonus, hyperkinetic and dyskinetic manifestations (athetotic and choreatic movements, tremors, etc.). Pronounced intellectual defect is present in all the cases; in the present material, two-thirds of the patients were at the idiot, and one-third at the imbecile level.

This disease seems to fulfill the initial condition required by mendelism, its biochemical characteristic constituting a unity in a biological sense. In the second place, the identification of the individual showing the character is made by exact laboratory methods, *i. e.*, the test for phenylpyruvic acid. Thus, a very clear-cut difference can be drawn between affected and nonaffected members of a family.

Jervis examined the urine of 20,300 mentally defective patients confined to training schools in a number of States, and of these 161 were found to show a positive reaction

The family of each patient was visited and all living parents and siblings were examined and tested for phenylpyruvic acid. Moreover, in a large number of cases other relatives of the patients, including uncles, aunts, and first cousins were examined. This resulted in the unearthing of 27 additional cases and information gained indicated that 25 more cases had occurred in the family groups but had died. On the basis of the data obtained, the author concludes that phenylpyruvic oligophrenia appears to be a clear illustration of a type of mental

deficiency determined by a single autosomal recessive gene.

The practical implications of this conclusion are that parents affected with phenylpyruvic oligophrenia should be discouraged from having other children, parenthood should also be discouraged in brothers and sisters, uncles and aunts of affected individuals, consanguineous marriages among members of families of patients should particularly be prevented and moreover, the patients should be segregated to prevent childbearing, since the great majority reaches sexual maturity.

The diagnosis of this condition from the laboratory standpoint is not difficult and can be readily carried out if the disease is suspected

Etiology

Schreiber¹⁰ states that careful examination of the paranatal records of mentally defective infants and children (for whom there was no history of inherited defect, infection or trauma unassociated with birth) has disclosed a definite relationship between fetal oxygen want and the later neurologic defect Since mental deficiency may occur as a result of cerebral anoxia, the controllable factors inducing asphyxia must be reevaluated. Foremost among these are the optional drug and anesthetic agents used to produce analgesia and amnesia in the mother. The asphyxia resulting from the excessive use of drugs to produce unconscious labor is no less serious in its effect on the baby than that from any other cause. Any optional method of delivery which produces a mentally defective infant has no compensation for the mother, the child or the physician

Sirkin,¹¹ in an analysis of 5 years' work with cerebral palsy points out that birth injuries occur much more frequently than meets the casual eye. The

predisposing causes which contribute to the incidence of birth injuries are prematurity, a rapid or precipitate birth, a long, slow labor, excessive molding of the child's head, a large head in proportion to the mother's pelvis, a malformed pelvis, improper use of forceps and unskilled obstetrics. He urges a conservative attitude in regard to the mental prognosis since the intelligence of some of these children may be actually higher than is evident while others never will be normal The future of each case has to be looked upon as a separate entity Brain damage severe enough to produce spasticity or athetosis, or both, will, in many cases, impair the intellect He emphasizes what has been pointed out by Carlson, that these cerebral palsy cases cannot be made into normal people, even if their mentality is normal. They will always have to be under more or less continued observation and guidance to maintain the level of improvement. On the other hand, if a hopeless bed patient can be taught to walk, speak intelligibly. dress himself, feed himself and take care of his personal needs, a great deal has been accomplished.

Treatment

Skeels and Dye¹² attempted to determine the effect on mental growth of a radical shift in institutional environment to one which provided superior stimulation. The experimental group included 13 mentally retarded orphanage children from 1 to 2 years of age, placed singly or by two's on wards with brighter older girls. The mean I Q for the group at the time of transfer was 64.3. As a contrast group 12 average and dull normal children (mean I.Q. 86.7) in an orphanage were studied.

Over a period of 2 years the mean level of intelligence of the experimental group increased markedly while that of the contrast group showed an equivalent decrease. The experimental group made an average gain of 27.5 points while the contrast group showed a mean loss of 26.2 points.

The authors believe that a change from mental retardation to normal intelligence in children of preschool age is possible in the absence of organic disease or physiological deficiency by providing a more adequate psychological prescription. Conversely, children of normal intelligence may become mentally retarded to such a degree as to be classifiable as feebleminded under the continued adverse influence of a relatively nonstimulating environment An intimate and close relationship between the child and an interested adult seems to be a factor of importance in the mental development of young children.

Foster, Brown and Bronstein¹⁸ studied the mental development in a group of dwarfish children whose physical underdevelopment was the result of (1) endocrine dysfunction, (2) bony and cartilaginous anomalies and (3) chronic and severe illness.

In the group with endocrine disturbances, marked deficiency in either the thyroid or pituitary gland produces marked retardation in physical development However, while severe mental retardation is associated with severe thyroid deficiency it is not, in the authors' series, associated with pituitary defect Their 1 case of achondroplasia was not definitely defective which they interpreted as meaning that mental deficiency is not necessarily associated with this In the group with chronic condition and severe illness there was no severe mental retardation However, the small children inevitably stature of these creates severe problems in their personality adjustment since they are usually treated as children much younger than

their actual ages and as a consequence are retarded in their emotional development. They may develop compensatory types of behavior. The type of adjustment which they make is probably dependent, to a large extent, on the way in which they are handled in the home and school situation.

Selling¹⁴ has stated that no one with any criminological experience would attempt to belie the statement that were all the feebleminded to be removed from the community, the crime picture would change remarkably and, as a matter of fact, a very large number of crimes would no longer be committed, or if they were committed, would be committed so sporadically as not even to constitute a social problem. He believes that the behavior of the feebleminded sex offender is somewhat different from that of the intellectually normal person since he acts at a more primitive level and some of his sexual misconduct is due to the fact that he has been unable to learn the social significance of such unacceptable conduct, that he is limited in his ability to acquire education and, hence, acts in a primitive fashion uncontrolled by either knowledge or self-acquired training Although all sex offenses cannot be laid at the door of the feebleminded, as seems to have been thought by various researches in the past, it would seem to be a very definite predisposing factor in the cases of a sex offense. Since the feebleminded lack the ability to remember what they have read or what they have learned through hearsay, when an impulse comes into their minds to commit a sex offense, the deterrent activity of hearing of previous sentence or discipline seems to be absent. The interesting observation was made that even though these feebleminded individuals may have been convicted of rape and the

evidence brought out against them markedly conclusive, they continue to deny their guilt.

Sterilization—In a paper dealing with a sterilization policy, Southwick¹⁵ discusses the sociological reason for terminating the existence of a portion of the germplasm of any society by attempting to determine the value to society of the germ plasm of patients committed to an institution for reasons of an "undifferentiated mental deficiency."

On the basis of the precept that any sound sterilization policy should be based upon a clear-cut demonstration that the germ plasm of the person to be sterilized must be distinctly deleterious to the welfare of society, a study was designed to determine the degree to which the intelligence quotient of persons institutionalized for the above reason might be considered as dependent upon hereditary factors. The study was based upon the records concerning 488 children of patients institutionalized at a

custodial institution. The investigation seemed to indicate that intelligence is an inherited, continuously variable, quantitative trait, produced by a large number of independently inherited allelomorphic pairs which, by dint of the large number of combinations possible, produce the innumerable quantitative gradations noted. Such a concentration of low I. Q. genes produces persons who are incapable of caring for themselves and so must be cared for by other members of society. To this extent, such genes are definitely and distinctly deleterious to the welfare of society.

Of the 488 children studied, there were records concerning the school attainments in 114 cases. Of these 45.61 per cent were patients in an institution for the care of the feebleminded, 36.84 per cent were definitely retarded in their school attainments and 17.54 per cent were in a grade normal for their age, but none had attained a grade in advance of that normal for his or her age

PSYCHOANALYSIS

By O. Spurgeon English, M D

Psychogenic Factors in Hypertension

Franz Alexander¹⁶ makes observations on the course of a systematic clinical investigation conducted at the Chicago Institute for Psychoanalysis. The objective of this clinical study was to explore the psychological processes and the personality structure of patients suffering from essential hypertension in the hope that a systematic study of the emotional life of hypertensive patients by psychoanalysis will throw some light upon the etiological rôle of emotional factors in the development of hypertension. Likewise, of course, the study aimed to see what possibilities existed

for treatment by psychotherapy in this condition. In the case studied, Dr Alexander attempted (1) to give a dynamic picture of the personality makeup of a hypertensive patient, (2) to correlate the fluctuations of his blood pressure with his changing emotional state; and, (3) to establish whether or not there were any specific emotional tensions which have a specific influence upon blood pressure.

To do justice to an article of this kind it will be necessary to quote the author freely in parts.

The patient studied was a married business man of Swedish descent with a

distinctive educational and family background. He had 4 children, 2 older boys and 2 girls. He occupied an important and responsible, but not the highest, position in a large concern. The physical examination of the patient revealed a well developed, well nourished, somewhat obese middled-aged man weighing 209 lb. During 2 years of observation and treatment of this 47-year-old man his systolic blood pressure fluctuated between 175 mm. and 136 mm. and the diastolic pressure ranged between 120 and 92 mm.

"When the patient was first seen he showed an extremely pronounced self-consciousness, with a vivid sense of inferiority He constantly compared himself unfavorably with others, had little confidence in himself, tended to undervalue his efficiency, was always doubtful about the merits of his accomplishments. At the same time he was very ambitious to excel, to turn out perfect work. He was definitely a retiring type, inconspicuous, a conformist, always polite, avoiding contradiction. His ambition to progress and to outdo the others remained restricted to his fantasy and did not appear on the surface It soon became evident that this overt attitude of modesty and compliance put him under an extreme pressure and created intense feelings of inferiority within him These became most tormenting in relation to his chief The patient never contradicted his chief, however, but would follow suggestions, accept blame while talking with him, but after leaving the office would be filled with self-contempt and would say to himself, 'You should have spoken up You should have said, no! You should have demonstrated to him that he was not right. You are no good and never will be any good' This self-depreciatory attitude usually became so unbearable that he would have the urge to drink As soon as the alcohol began to make its effects felt his spirits were lifted and he felt more courageous and stronger In this alcoholic mood he would also indulge in promiscuous sexuality in a rebellious spirit against limitations imposed upon him by external social standards and by the voice of his conscience. But while he was able to throw off his conscience while under the influence of alcohol his behavior was followed by remorse and guilt At home the patient's attitude resembled the one he showed at work. Here also he overtly subjected himself to all requirements of the marital state but he secretly rebelled against its restrictions.

"During the course of his psychoanalysis the deeper dynamic background was worked over. His rebellious, aggressive attitude against the social restrictions of marriage, against his boss. against routine-aggressive attitudes which he never could express openly and freely were the reaction to a strong, passive, masochistically colored feminine tendency and wish for dependence. As the analysis progressed more and more, unconscious, passive homosexual material came to the surface, both in dreams and in the transference. In his dreams he was usually attacked. In other dreams, women appeared in the masculine rôle, even equipped with male anatomy. These masochistic and feminine attitudes also came into expression in day fantasies in which he imagined his chief attacking, rebuking and abusing him By being abused and attacked he relieved his guilt feelings and at the same time obtained feminine, passive gratification. The guilt feelings came from his rebellious aggressiveness and extreme destructive competitiveness which were reactions to the deep passive feminine attitude. Fear and guilt blocked the expression of aggressiveness and the internally socially accepted standards prohibiting him from giving in to his wish to escape the struggle of life His aggressiveness and his protest against passive submission found a feeble expression in the adolescent behavior pattern-in surreptitious drinking and forbidden sexual acts

"The dynamic picture was one of an extreme polarization of the emotional life, on the 1 hand a wish toward the infantile rôle of dependence and the feminine rôle of submissiveness and passivity, counterbalanced by the opposite attitude of ambition, perfection and masculine superiority These 2 opposite tendencies mutually reinforced each other Alexander here points out that polarization of these 2 opposing psychological attitudes reinforcing each other in a vicious circle is very commonly found in neurotic persons and may even be a nuclear conflict typical for the contemporary neurotic in our competitive Western civilization. He points out that it exists in the peptic ulcer cases and in certain delinquent types He goes on to point out, however, that what made this hypertensive case so different from the peptic ulcer personalities or the delinquent types and other neurotics in which this

same vicious circle is a central issue, was the patient's extreme inhibition to satisfy either of his 2 opposing major trends. He could neither be satisfactorily aggressive nor as passive as he wished. The result was to give his analyst the impression of his being in a permanent emotional tension; a boiling volcano before eruption, but never erupting"

Dr. Alexander then presents a bird's eve view of the life history of the patient in order to see if there are certain parallel features in the developmental history of hypertensives. Noteworthy features in this life history were that as a young boy the patient was in every respect the outstanding member of the family His brothers looked up to him more or less as a hero. He could fight the battles of the younger boys He was inclined to extreme outbreaks of rage, was absolutely fearless, played an astonishing game of football and baseball. In his first 2 years of public school, he resented the routine which was then required and rebelled against 1 of the teachers quite violently His being sent home from school for unruly behavior became a regular occurence He still retained for a long time his superiority over his brothers and other boys. He was not only the best student in his grade, but probably the best student in the school The whole family and everybody who was in contact with him had the greatest expectations of him

"When he was 12 years old his father died. He felt he should cry as all the other members of the family did, but he had no true desire for it

"Gradually, the patient lost his leading position in the family Already in the first college years he began to slip, both in athletics and in scholastic achievements As a result he developed a severe depression. He was still an excellent student and a good athlete but both of his brothers began to catch up and even surpass him. In his high school days and college days the patient made friendships with socially outstanding boys, much wealthier than he was. When he finished college he obtained

a position in a concern owned by 1 of his friends' families. Leaning over backwards, he accepted in this company a menial position which was connected with extreme discomfort and even degradation. During this time he developed his second severe depression. Soon after he recovered from his depression, he married a socially outstanding girl and through this marriage he entered into a group much wealthier than his family. Although he obtained a very excellent business position, the patient had to struggle desperately to live up to the standards of his circle In the twelfth year of his marriage he started to drink, which was the only means of getting rid of his apprehensive depressive moods, which with great regularity every morning after awakening, began to torture him. Looking back on his life, back to adolescence, the patient was never free from a strong self-critical, depressive state of mind, which gradually grew worse and worse

"Viewing this history from a distant perspective, we see the gradual metamorphosis of an over-aggressive, successful, domineering young man, determined for leadership, into a shy, inhibited, conforming, overly modest and unexpressive person. The aggressive and courageous spirit of his early years appears in the adult only in the form of 2 neurotic behavior patterns—in promiscuity and drinking—in this typically adolescent way of showing masculinity and a tough independent spirit."

Dr Alexander goes on to give a more microscopic picture of the emotional development and thus the reasons for the patient's reaction found during the analysis between emotional tensions and fluctuations of blood pressure. He gives the figures and dates of blood pressure readings under 3 separate divisions, including when patient was calm, somewhat disturbed and very disturbed. At the beginning and end of every analytic session the blood pressure of this patient was measured by a mercury sphygmonionometer and compared with the emotional state of the patient and the details of the analytic material. The blood pressure was taken at first by a physician who did not treat the patient and then by the analyst in order to establish the influence of special emotional reactions towards the analyst. However, in the vast majority of readings there was no noticeable difference between the 2 readings. Furthermore, both observers took several readings.

These observations can be summarized as follows: In 201 sessions the patient's blood pressure was taken and compared with his emotional state. In 41 interviews the patients emotional state was very disturbed, in 99 interviews somewhat disturbed, and in 61 interviews the patient was subjectively calm.

His average blood pressure on the basis of all readings was 149/105. During the very disturbed interviews, the average blood pressure was 160/111 and in the calm interviews 141/99. There were only 2 very disturbed sessions in which he had a relatively low blood pressure, and both occurred on a day after he had consumed a considerable amount of alcohol. Otherwise the blood pressure functioned almost as a barometer of his emotional state, being high when the patient was emotionally disturbed and lower when he was calin

Because the patient came to a great number of the analytic sessions after consuming alcohol the question arose as to the direct effect of alcohol upon the blood pressure. In order to eliminate this complication, in the following chart only those blood pressure readings are considered which were taken when the patient was entirely sober.

There is no doubt that the dynamic nucleus of his emotional difficulties consisted of hostile impulses. These led to fear and guilt and as the next step to his depressions. His emotional condition could be best characterized as a state of inhibited hostile aggressive impulses.

In the last part of his analysis, the patient lost entirely his depressions, and

his emotional tension appeared only in the form of a tense feeling and some vague irritability. Most significant is the fact that during a period of 2 months which the patient's emotional difficulties were reduced to a minimum, when he had no apprehensions about his job, felt calm and contented, his blood pressure did not show the usual extensive fluctuations; his systolic pressure, with the exception of 1 day, did not surpass 150 mm.; in the last 3 weeks of this period, his diastolic pressure with the exception of 1 day never exceeded 100 mm. This is therefore significant, because viewing the whole period of the analysis, the variations of his systolic pressure were between 175 mm. and 136 mm. and of the diastolic pressure between 120 mm. and 92 mm.

While the analysis of the case was not entirely completed and all of the patient's tension relieved, nevertheless the author felt it was possible from the figures presented to conclude that if the analysis succeeded in further diminishing the patient's chronic emotional tensions that a good therapeutic result in the hypertension would have been obtained He finally concludes a definite correlation has been found between emotional tensions and fluctuations of the blood pressure. The nature of the emotional tensions has been identified as inhibited, but not deeply repressed aggressive impulses directed partly inward against the patient's own person in the form of depressions, partly turned outwards in the form of hostile feelings These emotional states were mixed with an apprehensive worrisome state of mind Finally, it was observed that during a period in which the patient was in an exceptionally calm state, his blood pressure was definitely lower and showconsiderably smaller fluctuations During the last period of treatment, with

the diminution of the emotional tensions, there was a slow but definite decrease of the day by day fluctuations, and a slow downward tendency of the average blood pressure level.

Leon J. Saul¹⁷ complements the work of Franz Alexander cited above and gives attention specifically to (1) the status of a particular conflict situation, and (2) the status of the hostilities.

This author found the central conflict situation to be strikingly similar in 4 cases. In brief this conflict situation consisted of (1) a masochistic submissive and an oral dependent attitude, originally toward a dominating parent, leading to a masochistic submissive attitude to a dominating conscience, to the parent of the same sex, and to parent-substitutes in later life; (2) chronic, unsuccessful, unsatisfied rebellion and hostility in protest against this submission. The rebellion and hostility were conscious or near to consciousness and not expressed directly because of fear of loss of love The submissiveness was not conscious and bitter hostility opposed making it conscious in the analyses. There was also rage at not getting the desired passive oral depend-\nother prominent ent gratification feature was excessive fear of heterosexuality, which was to some extent indulged despite the anxiety characteristic general feature of all of the cases was that both the oral dependent wishes and the hostile aggressive impulses were internally inhibited and were never satisfied in life or in symptoms These patients were neither passive and dependent nor hostile and aggressive. They could give in to neither trend During periods when they could and did, their blood pressures were markedly lower.

The author gives a few case histories and then compares these cases with other types as controls. He says, "it is

clear that dominating parents are common and that the conflict described is a general one and is not peculiar to cases of essential hypertension. However, pending further study of these and many more cases, the present material suggests that the status of the conflict may be peculiar to cases of essential hypertension. These patients submit, but they stifle intense hostility which is near to consciousness. As controls, it is easy to observe patients without hypertension who have this same conflict situation but who solve it in other ways. For example, one patient shunned situations in which his submissiveness would be stimulated. by doing independent free lance work. saying frankly that he was unable to work for a boss. He relieved unavoidable tensions by gambling in which he indulged with very little conflict. other cases, the submission is accepted with very little protest or with some narcissistic compensation. A comparison has not yet been made of the psychology found in essential hypertension with that found in angina and in the cardiac arhythmias The first impression is that the hostilities in the latter cases are freer, as seen in the dreams. In a small series of 8 controls, I have not found hypertension in patients who have the same conflict as the hypertensives but who have workable solutions for it. Thus, so far as the control series has been examined, no essential hypertension has been found in cases in which (1) the submissiveness is accepted, (2) the problem is avoided by shunning submissive situation, (3) the rebellion and hostility are adequately repressed and bound by organized neuroses or find adequate outlets in life behavior or sexual activity by assuming forms which are not too conflictful and anxiety producing for the individual, or, possibly (4) the hostility does not arise from this

protest situation, but from another source, for example, direct oral thwarting, but this is questionable."

He describes the status of the hostilities as both intense and chronic.

"However gentle the exterior, the analyses made it clear that these individuals were chronically boiling with rage. The hostility was in all these cases the central issue of the analysis, the pathogenetic element so to speak The psychological level of the hostility may be of importance since in all these cases it was close to consciousness. There is reason to suspect that the crucial point here may be the proximity of the hostilities to motility The hostility was in all cases very inhibited. On the surface these individuals were non-hostile and even overly gentle, but did not lack energy They worked, in fact often overworked, and succeeded, while protesting against doing so The hostility found no adequate outlet in behavior in life, through drainage by sexual activity (which often discharges unconscious sadistic impulses) or even in dreams, although there was apt to be considerable conscious hostile fantasy Although inhibited, the hostility in these cases was not adequately bound in an organized chronic neurosis, for example, paranoia, compulsion neurosis, chronic alcoholism, etc

"An attempt is made to describe the common psychological features in 7 cases of essential hypertension. The prominent similarities are (1) the prominence in every case of a dommating mother, with submissiveness and oral dependence toward her, transferred in the cases of the 2 men to their fathers; with consequent chronic, hostile, unsuccessful, nearly conscious rebellion against the submissiveness and chronic unexpressed rage at unsatisfied oral demands and at independent activity and work, (2) marked inhibition of heterosexuality, although indulged to some extent despite anxiety, (3) the status of the hostilities-intense, chronic, inhibited, near to consciousness and perhaps to motility, not adequately expressed, and not adequately repressed and bound as by an organized neurosis, (4) the mability to accept and satisfy either the passive dependent wishes or the hostile impulses, so that these individuals were neither weak and dependent nor aggressively hostile but were blocked in both directions. During periods when either trend was more satisfied, the blood pressure was markedly lower

"These results are more than suggestive but the series is too small as yet to establish conclusively whether or not these psychological features are generally typical for cases of essential hypertension."

Psychogenic Factors in Asthma

Twenty-four cases of bronchial asthma were analyzed at the Chicago Institute for Psychoanalysis over periods of 1 to 26 months. 18 Of these 6 were men. 10 were women and 8 were children. 4 boys and 4 girls. The cases chosen were patients in whom allergic hypersensitivity had been previously demonstrated by means of allergic hypersensitivity, allergic history, skin tests, etc., as judged by an experienced allergist. In addition Dr Siegfried Bernfeld supplemented the studies by analyzing and summarizing the case records of 8 asthmatic children who had been under close observation since birth by the Institute of Child Welfare at the University of California at Berkeley.

Dr French points out that psychoanlysis tends to mobilize and to throw into relief emotional conflicts which previously were latent, and 1 of his aims was to inquire whether there were conflicts of specific character in this condition

Upon passing the cases in review, the first impression was that they varied considerably both in their personality traits and in the type of emotional disturbance for which they sought treatment Many of our patients were particularly good children and were characterized in adult life by an urge to help and give to others. Some of our children's cases on the other hand were brought to treatment because of their particularly aggressive behavior. In 1 of our adult patients and in 1 of our children the picture at the beginning of the treatment was of a compulsive character with mild compulsive neurotic

symptoms. Still another, a man, sought treatment originally on account of conscious homosexual impulses. Upon superficial examination, therefore, there seems to be a considerable range of divergence in the personality picture presented by our asthma patients.

Upon deeper investigation, however, similar conflicts and reactions to them were found. The patients frequently found themselves awakening from a dream in an attack of asthma. In each case the patient was exposed to a temptation which threatened to estrange him from a parental figure, usually the mother. Moreover these patients had great difficulty in revealing unconscious material, even in symbolic form in dreams. Over and over again these patients would become blocked just at the point where the unconscious material was leading up to a confession. They feared to make this confession and woke up wheezing At the same time the urge to confess is rather strong and they want very much to regain the love of parental figures by confession.

"Incidents of this sort occur frequently in the histories of our asthma patients. So long as this technic of winning back reconciliation with the mother by confession is successful, the patients appear to be protected from asthma attacks. But sometimes one is afraid to confess. Then as in this dream the confession is choked in one's throat and in its place occurs an asthma attack.

"Confession is a defense that utilizes speech and speech is a respiratory mechanism. It is therefore perhaps not surprising that it should have so intimate a relationship with the asthma attacks. It is interesting to note moreover that there seems also to be a very intimate relationship between asthma and crying or laughing. There is much to suggest, in fact, that the asthma attack is really a sort of equivalent of a cry of anxiety or rage which has been inhibited and repressed. One of the first reactions of the child upon separation from the mother at birth is to cry and during early infancy and

even later, crying remains the predominant reaction of the child in situations of helplessness when he can only wish for the mother to return to him. In later life this primitive cry is modified into speech and in confession retains the function of maintaining the bond between the child and mother. For some reason, in the situations which provoke asthma attacks the child is unable to cry. Some of our patients state that they have not cried for years and others boast that they have never been afraid In other cases it is apparently only in certain situations that crying is inhibited. Of particular interest, however, is the fact that we are sometimes able to observe the cessation of an asthma attack and the appearance of crying in its place. Such replacement of asthma attacks by crying is particularly apt to occur at times when the analysis is beginning to achieve some degree of resolution of the asthma attacks"

The author then goes on to discuss ways in which the asthmatic tries to defend himself against anxiety One of these is through winning love through compliance and giving to others. Another is through capitalizing on their symptom, still another by mastery of the anxiety through acting out by sexual activity Children often try to defend themselves from anxiety by aggressive behavior which wards off the dangerous temptation Another is by adapting an impersonal and detached attitude toward life Apropos of this particular mechanism of defense as well as others, the author says that in connection with these withdrawal mechanisms it is interesting to note the reactions of our asthma patients to the danger of actual physical separation from the mother. It would seem that most asthma patients are particularly prone to attacks of asthma at times when they are undecided or in conflict as to whether or not to leave some mother figure. In the analysis we were early struck with the fact that asthma attacks tended to occur predominantly on weekends or during the period just preceding

more prolonged interruptions of the analysis. Interestingly enough, during vacation periods, after the first few days. the patients were often singularly free from attacks. Then just prior to resumption of the analysis the attacks would again begin to occur. In the history of these patients also there would tend to be a relative freedom from attacks during periods when the patients had actually achieved a physical separation from their mothers. It would seem that the precipitating situation is not the actual fact of separation from the mother but the indecision and conflict between the urge to cling to the mother and the need to separate from her.

In his conclusions Dr. French included some observations he had made upon the relation of psychological and allergic factors to each other as follows: First we have seen that asthma attacks tend to be precipitated by emotional conflict situations of a rather uniform and typical character. It would seem extremely improbable that these emotional conflict situations should in every case have coincided with an allergic stimulus which was absent during the often rather prolonged periods during which the same patient's emotional withdrawal from the analysis was marked and during which he also was free from asthma attacks Moreover a few patients experienced an initial relief from asthmatic attacks upon starting the analysis due apparently to reassurance resulting from analyst's interest in them and most of our patients developed an aggravation of the frequency and severity of their attacks as the analysis, after working through the defensive mechanisms, approached the fundamental conflict that we have been describing. In a few cases whose attacks had been confined to a particular season, asthmatic attacks appeared during the analysis also during other seasons of the year.

In some cases the substances to which the patients were allergically hypersensitive proved also to play a significant rôle in their psychological material. A patient whose skin test was strongly positive for ragweed recalled that at the age of 6 he had lost his brother in a hay field where the brother remained all night before he was found. During the analysis the memory of this incident was frequently accompanied by severe wheezing. Other patients who showed marked hypersensitivity to cat hair also dreamed frequently of temptation situations in which the temptation was symbolized by a cat. Still another patient who expressed a violent conscious resentment of children displaced the greater part of her normal maternal interest upon cats and upon test developed an extreme allergic reaction to cat hair.

Finally, in a number of patients as a result of analytic therapy the asthmatic attacks were greatly relieved and we could observe during the analytic sessions the gradual replacement of the asthmatic attacks by crying and then by a diminution of the fear of sexual temptation

One patient who had previously shown a marked sensitivity to horse dander and in whom horses regularly elicited attacks of asthma later became able to ride horseback without any trace of asthma

All these observations would suggest that psychological and allergic factors probably stand in a somewhat complementary relationship to each other in the etiology of bronchial asthma, that in some cases asthma attacks may be precipitated by allergic factors alone, in others by emotional factors alone and that in still other cases cooperation of allergic and emotional factors may be necessary to produce the attacks.

THE PSYCHIC COMPONENT IN CARDIAC, DIABETIC AND FRACTURE PATIENTS

By Joseph C. Hughes, M.D.

Dunbar and her associates¹⁹ in an analysis of 1200 cases of cardiac, diabetic and fracture patients stress that the best care for the chronically ill is not always provision for special care, relief from responsibility and a restricted regime. They state that in their experience they have observed many patients who have been handicapped in their recovery from organic illness by such procedures because the psychic and not the somatic factor was primarily responsible for the prolonged duration of the illness.

Psychic factors played important rôles in 79 per cent of their patients. As these authors point out the development of the habit for chronic illness in cases of heart disease, diabetes, fractures and other prolonged illness depends upon the patient's personality and the effectiveness of the physician in appreciating his patient's psychological motivations. These psychological factors will be apparent to the physician if he looks for them, at the time of the first examination. They

can be estimated by observing the patient's attitude and reactions to himself, others to his illness and to life in general. More specific information can be had by noting from the patient's own description of himself of the rôle played in his illness by anger, resentment, impulsiveness, ideas of guilt, punishment, love, hatred, aggressiveness, etc.

Once the physician has a knowledge of his patient's personality, the management of his illness should be directed in a manner to avoid either excessive spoiling or severity in order to avoid the occurrence of unfavorable impulsive behavior on the patient's part if the patient has neurotic traits these should be treated as well as his physical illness. Third, an attempt should be made to prevent the development of repressed feelings in the patient by permitting him to discuss his ideas. Fourth, the patient's emotional interests should be kept centered on the idea of being well.

TREATMENT IN THE PSYCHONEUROSES

By Louis H Twyeffort, M D

General Psychotherapy

Although the "obsessive-ruminative tension states," when fully developed, provide some of the most difficult psychiatric problems in terms of alleviation or cure, considerable amelioration or relief may be brought about when these tendencies are checked earlier, before their full-blown symptoms bring these patients to consult the psychiatrist. Some of the simpler forms of therapy which

may be of help in some of these cases are set forth in a comprehensive approach to the subject by L. F. Woolley.²⁰

Psychogenic disorders in childhood frequently simulate organic disease and often lead to unfortunate mistaken diagnoses W. A Hawke²¹ reviews 12 cases of this kind, and sets forth briefly the etiological factors of psychogenic import which may give rise to these conditions He lists methods of investigation which

lend themselves to the general practice or hospital milieu and discusses very practical modes of therapy. Among the more important contributory psychogenic factors in such cases are the following: (1) Difficulties in school adjustment rarely secondary to intellectual inadequacy; (2) specific reading difficulties; (3) unstable parents unable to handle the problem presented by the child at home because of their own emotional immaturity; (4) mismanagement of the illness because of the constant attention of oversolicitous parents which engenders bitterness in the child. In most cases the physical symptoms are the physiological expression of the strain associated with the undesirable situation

"Industrial or Occupational Neuroses"-M. Culpin²² maintains that individuals with so-called "occupational neuroses" (e. g., writer's cramp; miner's nystagmus, etc.) often show many other neurotic symptoms and trends if ade-With reference to quately studied "nuner's nystagmus" in particular, he feels that the presence and degree of oscillation is wrongly insisted upon as a diagnostic criterion of incapacity since oscillation itself may cease and other associated symptoms remain or become aggravated. In certain coal mines as high as 35 per cent of the workmen using safety-lamps may show oscillation of the eveballs but as a rule are unaware of it and make no complaint (Cause probably physiological, due to exposure to illumination below that necessary for foveal vision) According to statistics, only about 1 of this 35 per cent will complain of symptoms "The question is never asked why the other 34 escape trouble" In the "traumatic neuroses" of industry "grant of compensation without adequate understanding of the patient's condition is almost invariably We must to his disadvantage

beware of easy acceptance of the belief that such cases . . . recover when a final settlement is made." The author quotes Halliday as pointing out that an analysis of initial diagnoses in incapacitated insured workers reveals only 2 per cent of such individuals diagnosed as psychoneuroses, whereas an examination of 1000 people drawing sickness benefits reveals the incidence of psychoneurotic disabilities at 33 per cent. Mention is also made of the marked correlation between neurotic trends in workers and their tendency toward excessive accidents. Recent statistics tend to show that industrial accidents are not so much a matter of chance as was formerly believed. T. A. Ross²³ is inclined to feel that "it may be stated with confidence that there are no 'traumatic neuroses;' there are only compensation neuroses with trauma in the history." As he suggests, there are no "traumatic neuroses" after hunting or skiing accidents in which there is no question of compensation The physician should warn a patient contemplating the seeking of damages that the anxieties inseparable from litigation. will probably of themselves bring on disturbing symptoms, and that worry over the constant postponement of settlement is liable to keep him ill. As Ross points out, under the present industrial set-up in which work is frequently laborious and distasteful, and sickness insurance compulsory, illness may be made too easy and the patient then dreads returning to the job. This dread is less balanced by the fear of starvation than it was in former days Therefore neuroses can be added to physical disease

Special Forms of Therapy

Group Therapy—The results and problems of group psychotherapy is discussed in stimulating fashion by P Schilder ²⁴ He is inclined to feel that

some patients do better under such management than when seen individually. In such a setting the patient seems nearer to reality, since the emotional interplay is between him and a group, rather than between him and a single person—the therapist.

An outline of psychotherapeutic procedures which lend themselves readily to the handling of neurotic patients in general practice is set forth by J. L. McCartney.²⁵ Special reference in this article is made to the judicious use of hypnosis in certain cases.

Shock Therapy—With the encouraging results which have been reported over the past 4 years in shock therapy applied to the psychoses, it is but natural that such a therapeutic weapon should have also been tested in the treatment of the severer neuroses Shapiro and Freeman²⁶ report a series of 30 cases of psychoneuroses treated chiefly with metrazol, though a few of the patients received insulin. In this series there were 7 cases of obsessive-compulsive (psychasthenia), 6 anxiety neuroses, 7 reactive depressions, 5 conversion hysterias and 3 cases of chronic hypertension. The following result is claimed Recovery, 15; improvement, 9; failure, 6 The authors do not claim any alteration in the personality of these patients, nor the elimination of the situational or emotional difficulties "But in the majurity of cases after from 3 to 10 convulsions the patients no longer suffer from the complaints that brought them to the physician" The chief therapeutic result seems to be a relief of tension followed by the disappearance of secondary phenomena such as obsessive thinking, fear, insomnia, hysterical palsies, etc. Freed of emotional tension, these individuals are subsequently able to adopt a more rational attitude toward their problems and to make better use of their

own capacities in working out more satisfactory life readjustments. These workers recommend that probing after treatment be avoided. Sagebiel²⁷ reports a series of 7 cases of severe neuroses similarly treated, who had failed to respond to any previous therapy. As a group these neurotics seemed more resistant to the convulsive reaction of metrazol than a comparable series of psychotic patients. The following results were claimed: 1, complete remission; 4, partial remissions; while 2 cases showed no improvement. Sagebiel believes that the effective factor in this form of therapy resides in the production of "an artificial, controlled death threat" directed at the "primitive centers of the selfpreservative instinct which dislodges the individual's interest from their former somatic or psychic overpreoccupation" He also feels that this form of therapy may act principally "as a powerful method of suggestion," which nevertheless brings about certain definite changes in the personality, possibly because the primitive instinctual drives are thus further compelled to respect accepted social standards

In a comprehensive review of the treatment of *insomnia*, L. J. Karnosh²⁸ mentions various pharmacological procedures which may act as useful adjuncts in treating sleeplessness in psychoneurotic states Though, as the author states "a mental aeration is far more valuable than a sedative," the use of certain of the newer vitamin preparations have been helpful in relieving neurotic insomnia He mentions the quieting effects of the hypodermic injection of ½ grain (10 mg.) of crystalline vitamin B_1 every other day and the oral administration of 2½ drams (10 Gm) of brewer's yeast every day. Large doses of ascorbic acid are also said to yield gratifying results The dosage suggested is from 15 to 45 grains (1 to 3 Gm.) of 1-cevitamic acid daily. Also, "in view of the propensity of old people to deficiency diseases, massive doses of vitamin B₁ and C should be given to stave off the insomnia incidental to cerebral arteriosclerosis and to senile decay." E. L. Richards,29 in considering the psychiatric aspect of vitamins, emphasizes the fact that vitamin B₂ (a flavine), apparently acts as an enzyme of internal respiration, the lack of which may lead to anoxemia of brain tissue For this reason the administration of vitamin B complex may be indicated. The B₁ component is essential to the utilization of glucose by brain tissue. (B₁, thiamine, is the antineuritic, antiberiberi, heat-labile fraction of vitamin B which is found in yeast, unpolished rice or bran)

Various Pharmacological Aids— Stressing the fact that the physiological causes as well as the fundamental psychological factors must be recognized in psychoneurotic states, W. J Kerr, et al 30 lists various adjuvants in the treatment of anxiety syndromes These workers suggest various means of experimentally producing or intensifying the symptoms by simple pharmacological procedures and then temporarily elimmating them by other simple physiological means "The physiologic mechanism can be proved by reproduction of the symptoms and the patient's confidence thus gained. There is then no necessity of telling the patient that he is 'just nervous'" The next step consists in helping the patient to recognize the relation of his emotional conflicts to his physical symptoms Thus, when a patient presents a hyperventilation syndrome it is suggested that he be instructed to overventilate (usually less than 3 minutes) until some of his customary symptoms reappear. He is then made to overbreathe air to which 2 to 5

per cent of carbon dioxide has been added, as a result of which the untoward symptoms are usually relieved in a half minute. In some patients hyperventilation is reduced by teaching them to breathe abdominally and also may be helped by the administration of ammonium chloride (up to 45 to 90 grains-3 to 6 Gm.) daily in divided doses to help bring about a relative state of acidosis. Dilute HCl in small doses and an acidifying diet may help. Nevertheless the removal through psychotherapy of the cause of the anxiety should receive primary emphasis. These adjuvants to therapy may also be of help in the handling of "effort syndrome." Certain members of the atropine series may prove especially useful in the treatment of spastic colon frequently encountered in the anxiety states. The new synthetic drug "Transentin" may here prove effective. Nevertheless the authors stress that spastic colon is rarely found in individuals with normal psychological adjustment. The prescribing of dietary measures in such cases is therefore not directed at the fundamental pathology

J. F Quinlan³¹ discusses the contributory physiological rôle which hypoglycemia may play in bringing about anxiety states, as well as the fact that mental states in which anxiety or apathy are prominent features may in themselves contribute to the appearance of low blood sugar levels. Such low levels may be the result of emotionally induced faulty absorption through the gastrointestinal tract. For these reasons the exact blood sugar status of all anxiety patients should be determined. Since chronic low blood sugar levels may result in defective cholesterol catabolism, the direct final result may be in the nature of arteriosclerotic changes and other visceral alterations seen in the various degenerative diseases. Thus the correction of low blood sugar

levels in chronic anxiety states becomes a matter of especial importance.

SKIN

In discussing the rôle of emotional factors in pruriginous lesions, H. Kelman and H. Field³² emphasize that "a skin disease, or in fact any disease, cannot be considered apart from the patient who suffers from it" Emphasizing that the skin acts as an organ of emotional expression, they review in detail 3 cases of eczema of a pruriginous nature and place emphasis on etiological factors of an emotional nature which as long as they were unappreciated made for lack of therapeutic success in the handling of these cases. The method of approach to the patient who may be unwilling to see the need of psychotherapy in his case is discussed

ASTHMA

A series of 50 cases of bronchial asthma has been studied in detail by A T. McDermott and Stanley Cobb³³ from both a medical and psychiatric approach. Complete protocols are given These cases were taken from an allergy clinic without selection and interviewed psychiatrically. Seventy-four per cent seemed to have a definite emotional component back of their asthmatic attacks. Thirty of the patients showed neurotic traits, usually of a compulsive character. Of the neurotic group only about 20 per cent had been helped by drugs and biological products.

As the result of a survey of 24 cases with bronchial asthma who have been psychoanalyzed, T. M. French³⁴ discusses the specific common characteristics of the emotional situations which seem to precipitate the attacks. A common finding is a conflict engendered by

the individual being exposed to a temptation which would estrange the patient from a parental figure, usually the mother, exposing the person to the potentiality of losing the parent's love. The nature of the situation is frequently a sexual temptation. In these patients nocturnal attacks are frequently precipitated by a dream centering around conflict between an acute temptation and coincidental fear of losing the parent's love In several cases the analyses suggested that sexual temptation rather than actual indulgence in forbidden sexual gratification precipitated the attack—i. e., the element of indecision as against the overt accomplishment Other factors, besides sexual temptation, which seem to precipitate attacks were the birth of vounger siblings, or the discovery of the mother being pregnant—situations which were interpreted by the patient as threats of loss of the mother's love. Several of the male patients had continued sleeping in the mother's bed until after puberty.

Unconscious defense mechanisms which seemed at work during symptom-free periods were as follows. In younger patients attempts at being particularly good children, efforts to use sickness and suffering as a means to regain the sympathy and affection of the parents (to assuage the guilt feelings); occasionally the child may use the asthma attacks themselves to regain the mother's love The central conflict seems to center definitely around an attempted solution of the oedipus situation, and the precipitating factor is not connected with the actual fact of separation from the mother, but with the indecision and conflict between the urge to cling and the need to separate In some of these cases the substances to which the patients were allergically hypersensitive also played a significant rôle in the psychological material, the appearance of which psychological material would at times in itself precipitate an attack. In a number of these patients the asthma attacks were greatly relieved by psychoanalysis with no other coincidental therapy. The author concludes that some cases of bronchial asthma may be precipitated by allergic factors alone, others by emotional factors alone, and in still other cases both factors may cooperate.

In discussing the emotional component in bronchial asthma, C. H. Eyermann³⁵ emphasizes the psychic influence in some of these cases and brings attention to the interesting findings in pneumographic records of the relation of mental to respiratory functions He would be inclined to view bronchial asthma as "a reaction pattern which can be activated by many kinds of stimuli along facilitated pathways" In these cases he is of the opinion that psychotherapy "mostly as persuasion and suggestion, will help, not in the sense that it removes the cause but rather as part of a reeducational program The allurement of the allergen should not cause us to forget the patient, for the psychotherapeutic plan depends upon what kind of a patient has the disease"

CARDIOVASCULAR SYSTEM

A review of much of the recent literature on "Cardiovascular Neurosis" is presented by J. L. Caughey, Jr. ³⁶ He is inclined to view this clinical entity as a "syndrome arising from complicated alterations in the total personality of the patient" Only careful clinical and laboratory study permits its separation in terms of physiological manifestations from those of actual organic disease. In many patients the symptoms appear to have been "precipitated or perpetuated by faulty medical supervision of the difficult problems involved". A considerable

part of treatment involves "a reconditioning of the individual's interpretation of, and response to, afferent visceral impulses." This syndrome may frequently coexist with actual organic heart disease. Various tests which help in the establishment of the differential diagnosis are discussed.

Specific Character Traits in Individuals with Cardiovascular Symptoms-Interesting findings along specific character trends or personality patterns are stressed in F. Dunbar's 37 detailed analvtical study of a large number of patients suffering from essential hyper-"rheumatism" and coronary tension, disease Chronically pent-up emotions of fear and resentment figure extensively in the personality study of cardiovascular The characteristic psychological defense of this group of patients seems to reveal itself dramatically in variations in the degree and type of muscle-tension. More specifically, this author refers to muscle tension as "a borderline between instinct and outer world, restraining aggressive action towards the latter and binding vegetative energy" In patients with cardiovascular diseases there is frequent evidence of generalized smooth muscle spasm This condition of generalized tension may escape attention because such individuals frequently give the external appearance of quiet control Psychoanalysis of these individuals usually reveals that they are likely to deny that they are "nervous," partly because they are universally afraid of their repressed aggressive impulses which only become clear on analysis The large cardiovascular material studied (exclusive of cardiovascular syphilis, subacute bacterial endocarditis and congenital lesions) presented rather specific differentiated peronality patterns and unconscious reaction trends depending upon whether the presenting syndrome was

being characterized chiefly by: (a) Hypertension; (b) exaggerated dyspnea and palpitations, (c) marked pain (i-anginal; ii-joint pains).

- (a) Hypertensive Syndrome—Personality trends as shown by psychoanalvsis-Exterior behavior characterized by a considerable degree of self-control and reserve. Few outspoken neurotic symptoms. Existence of suppressed chronic rage as revealed by temper tantrums in childhood with the emotion of anger later completely repressed or expressed in less obvious acts of rebellion. Opposite characteristics (placidness, calm exterior, etc) seem to develop on a defense basis, coupled with marked submission to authority. There is also marked conflict with overpassive tendencies and neither the submissiveness nor the hostility are given adequate expression. As the result, these individuals are always tense Analysis is said to greatly lessen the tension As the underlying conflict is brought up and worked through, the defense mechanisms are no longer necessary and in a number of cases the high blood pressure has returned to normal
- (b) Syndrome Characterized by Dyspnea and Palpitation - Findings during analysis: "Pseudo-hereditary" factor very important even in patients with actual organic lesion, many of the patients giving a history of childhood propinguity to cardiac relatives. Diseases of childhood often play an important rôle here in giving psychological prominence to certain types of symptoms. Frequent unconscious tendency to identification with the mother, and attitude toward parent is one of submission Often associated dreams of smothering. Existence of claustrophobia. As with the hypertensive group symptomatic relief is sometimes readily brought about by superficial psychotherapy in these cases

Also, poor sexual hygiene frequently adds a marked element of anxiety neurosis in these individuals which is also amenable to psychotherapy.

- (c) Syndrome Characterized by Joint Pains—Recurrent findings in the psychoanalyses of these individuals are as follows: A tendency to symbolization of the sites of pain; rather typical fantasy life,—the focal conflict relating to the sexual rôle: Conflicts over masturbation; fear of mutilation or death as punishment therefor, conflict over sexual rôle (the girls being inclined towards tomboyishness, the boys towards passivity). Their somatic symptoms seem to have a psychic meaning,—are incapacitating and of a punitive nature
- (d) Syndrome Characterized by Anginal Pains—Whether the patients suffer from coronary disease or from pseudo-angina the unconscious attitudes are markedly related to repressed hostility expressing itself somatically in vascular and muscular spasms. In addition, the unconscious trends also center around a prominent sense of guilt and a tendency toward self-punishment On a more superficial level these individuals show a tendency to hold grudges, to enjoy revenge and their dreams are frequently replete with hostile themes. Through psychoanalysis many of the cases studied have been enabled to work through the basic conflicts with a resulting relief in the disturbance in muscle tension with coincident marked improvement of symptomatology In a number of cardiovascular cases tending toward decompensation, the frequency of such decompensated states has been greatly reduced

"ESSENTIAL" HYPERTENSION

The present conception of "essential hypertension" has been thoroughly re-

viewed by L. N. Katz and L. Leiter³⁸ in a detailed correlation of present day psysiological and clinical knowledge of this disease picture. "To neglect the fact that patients with high blood pressure have mental conflicts and emotions" is as serious an error as to ignore the physiological aspects of blood pressure control. In our ignorance of the true etiology of this condition treatment becomes a difficult matter as there is "so little known or understood of what is to be treated." Various therapies have been invoked from time to time: Dietary treatment; general hygienic measures; surgical denervation of the kidneys; splanchnectomy or thoracicolumbar sympathectomy. Recent attempts to approach this syndrome from a psychological viewpoint via psychoanalysis have suggested the presence of unresolved emotional conflicts, which when treated have been followed by clear-cut clinical improvement

F. Alexander³⁹ in outlining a tentative hypothesis concerning the emotional factors in essential hypertension, points out that the conclusion of most authors is to the effect that whatever organic findings appear in long-standing cases are in the nature of secondary changes produced by the hypertension rather than determining its development "In discussing the problem of etiology, it is important to differentiate between mechanisms and causes" The neurogenic and the humoral theories of the increased arterial tonus are not contradictory. They are to be considered merely intermediary mechanisms and not etiological. The influence of acute emotions upon the blood pressure has long been established as a clinical fact Intensive psychoanalytical study of the series of patients with essential hypertension strongly suggests that "chronic, inhibited, aggressive hostile impulses . . have a specific influence

upon the fluctuation of the blood pressure" of these individuals. These studies further strongly suggest that such patients have "a characteristic psychodynamic structure" consisting of "a very pronounced conflict between passive, dependent, feminine, deceptive tendencies and overcompensatory, competitive, aggressive hostile impulses which lead to fear and increase a flight from competition towards the passive, dependent attitude." Although this vicious circle is a common central emotional conflict in a large number of neurotic individuals with normal blood pressure, yet this nuclear complex in the hypertensive individual differs principally in his "inability to receive freely either one of the opposing tendencies." He can neither "accept his passive, dependent attitude nor freely express his hostile impulses." "Our assumption is that a chronic inhibited rage may lead to a chronic elevation of the blood pressure" These analytical investigations are still too recent to permit any definite evaluation of underlying therapeutic possibilities. Nevertheless. the successful result in lowering the blood pressure, in some cases to normal, suggests that the psychoanalytic method may offer definite therapeutic possibilities "during the early fluctuating phase" before pathological vascular changes ap-E. Weiss⁴⁰ has presented a comprehensive review of recent advances in the pathogenesis and treatment of hypertension. Considerable emphasis is placed upon the suggested psychic factors and suggestions are advanced for the practical handling of these cases in general practice "We are too little concerned with the emotional life, which may hold the key to the satisfactory management of the hypertensive patient"

The common psychological features of 7 cases of essential hypertension treated by extensive psychoanalysis are recorded

by L. J. Saul.^{41, 42} These center around typical subconscious attitudes brought to light as the result of analysis. The characteristic picture, expressed in psychoanalytical terminology is as follows. Early in childhood the patient showed marked submissiveness towards the mother, transferred later in male patients to the father, thus making for a submissive situation against which the patient later was in constant hostile, unsuccessful rebellion. The other main reaction to the mother, seen in all cases, was the "oral, dependent attachment to her which formed part of the submissiveness and was rebelled against, but which, when not satisfied, due to both external thwarting and internal inhibition (guilt, pride, ambition, and narcissism) led to chronic rage at the frustration" A second important similarity was the "marked inhibition of heterosexuality, although indulged to some extent despite anxiety." The third important similarity centers around the "status of the hostilities"the gentle exterior covering over intense hostility, very much inhibited but close to consciousness, and neither adequately expressed nor adequately repressed or bound by any organized neurosis. The central theme centers around an "mability to accept and satisfy either the passive, dependent wishes or the hostile impulses, so that these individuals are neither weak and dependent nor aggressively hostile but are blocked in both directions. During periods when either trend was more satisfied, the blood pressure of these patients was markedly lower

As L. J. Saul⁴² also points out, a controlled series of cases with the same submissiveness conflict but *no* essential hypertension "were found to handle the conflict in other ways, such as accepting or overcompensating for the submissiveness, or escaping it successfully"

In view of the rather extensive litera ture centering around specific surgical procedures aimed at lessening the blood pressure level in cases of "essential" hypertension, the appraisal by I. F. Volini and N. Flaxman⁴³ of the effect of nonspecific surgical measures (e.g., hysterectomy, prostatectomy, cholecystectomy, etc) in the presence of essential hypertension, are interesting These workers conclude that the symptomatic relief and the reduction in blood pressure resulting from these underlying nonspecific surgical measures "are sometimes better than those obtained by specific procedures." The evidence presented justifies some doubt concerning the indication for and result of specific surgical intervention. The duration of the symptom-free stage in this series of 27 cases average 3½ years.

GASTROINTESTINAL TRACT

Reviewing the nervous relationships of the gastrointestinal tract, F Kennedy⁴⁴ lays considerable emphasis on the rôle which emotional stress may play in organic disturbances of the alimentary canal As the result of cortical or psychic influences the parasympathetic apparatus may be adversely affected "Vagus stimulation will cause increased motility and secretion, whereas sympathetic stimulation gives the reverse effect" Quoting Cushing he remarks, "The functional release of the vagus from paralysis of the antagonistic sympathetic fibers leads to hypersecretion, hyperchlorhydria, hypermotility and hypertonicity, especially marked in the pyloric segments" There may also be "accompanying local spasms of the terminal blood vessels, small areas of ischemia or hemorrhagic infarction" which may eventually leave the overlying mucosa exposed to the digestive effects of the individual's own hyperacid

juices. This is a possible mechanism in the formation of peptic ulcer,—emotional factors thus forming a significant link in the long chain of indirect cause and effect. The rôle of altered digestion, possibly on an emotional basis, with consequent faulty assimilation must not be overlooked as one possible origin of certain avitaminotic states.

W. C. Alvarez⁴⁵ points the way toward a better understanding of functional disturbances of digestion when he advises gastroenterologists to see their patients "as human beings in their setting at home and in the office." As this author warns, recognition that a patient's complaints are functional is not enough. The internist "must go further with his study until he knows what type of functional trouble is present and what is the cause."

Although gastrointestinal symptoms may in many instances be emotionally conditioned or may arise from lesions within the intestinal tract, the etiological factor of forces outside of the digestive tract must not be overlooked. H. Gauss⁴⁶ lays stress upon the fact that such symptoms in some instances may result from disease within the brain,—expanding intracramal lesions, epilepsy, migraine, syphilis Intracramal pathology may result in chronic dyspepsia, acute paroxysmal attacks of pain, or in the peptic ulcer syndrome but none of these signs is in itself pathognomonic of the etiological source of the disorder. E. G Billings47 commenting upon the experience of a large gastrointestinal out-patient department, states that over half of the patients seen show no demonstrable gastrointestinal or central nervous system disease He would look upon the abnormal motility and secretory phenomena as personality protests against the stresses and strains of life, and as being psychologically determined by the personality or the environmental situation.

In reviewing the histopathological changes of the nervous system in cases of peptic ulcer. A. R. Vonderahe⁴⁸ concludes that the nervous system usually shows characteristic lesions once a severe ulcer is established. He feels that many of the characteristic symptoms of advanced peptic ulcer cases (e.g., ascending pulse rate) may result from punctate hemorrhages of the dorsal motor neucleus implicating the cardiac neurons He would thus explain many of the symptomatic sequelae following severe ulcer as depending on injury of parasympathetic centers in the dorsal vagal motor nucleus, as well as in centers in the thalamus and hypothalamic areas

Mucous Colitis

B. V White, Stanley Cobb, C. M. Jones⁴⁹ have presented in monograph form their combined medical and psychiatric studies of 60 cases of mucous colitis In addition to an extensive clinical discussion of this syndrome the experimental production of lesions is reviewed, the psychological considerations are presented in detail with adequate and extensive case histories, the personality factors evaluated and therapy discussed especially in terms of the newer psychological implications As their thesis they conclude that mucous colitis "is a physiological disorder of the colon brought about through the action of the parasympathetic nervous system and that liberation of cholinergic substances accounts for the lesions" In addition to certain physiological and pathological states which seem to predispose the individual to develop the localized lesions of this condition, the authors feel that the commoner source of parasympathetic overstimulation is emotional tension. Certain specific characteristics of the personality

seem to predispose to this development of tension,-"over conscientiousness, dependence upon the opinion of others and sensitivity." Such traits lead to the development of ready anxiety when situations arise in which the individual is open to criticism as well as to feelings of guilt. Such people also readily develop extreme degrees of resentment. "The 3 emotions, anxiety, guilt and resentment, are those most commonly associated with tension in patients with mucous colitis" In addition, these individuals tend toward obsessive methods of thought which enhance their constant preoccupation with their problems. Though fear ordinarily activates the sympathetic system and anger more readily excites the parasympathetic system, when both these emotions were present, resentment seemed the more prominent. As a therapeutic program helpful in the majority of instances the authors have formulated the following approach: (1) The establishment of rapport—"in no group of patients is this more important" (2) A meticulously careful history (3) Establishment of the diagnosis beyond doubt. (4) Explain to the patient that his symptoms are due to overexcitability rather than to torpor of the bowel, desensitizing the patient simultaneously from his customary laxative habit (5) Outlining the various factors physical and emotional which increase the irritability, spasm and mucous secretion of the intestines (6) Establishing a daily program of activities which will minimize undesirable factors. (7) Importance in regularity in bowel movement must be minimized (8) The rôle of tension in aggravating the disorder must be emphasized,—often illustrating with examples of other patient's experiences. (9) Having unearthed the cause of the patient's tension, the use of various psychotherapeutic technics are available to give the patient true insight. In addition social service adjustment and "reassurance and transference psychology" may be of help.

E. G. Wakefield and C. W. Mayo⁵⁰ again emphasize how cure in functional disorders of the colon is "not to be sought merely in certain dietary rearrangements or in merely treating the colitis" but that success lies in attempts to control scientifically the adverse social factors.

Anorexia Nervosa

R F. Farquharson and H. H. Hyland⁵¹ characterize this illness as a metabolic disorder of psychological origin. In their survey of 8 cases they place emphasis on "the typical syndrome of emaciation, amenorrhea, low basal metabolic rate, low blood pressure and often rather low fasting blood sugar values with flat sugar tolerance curve" This syndrome develops as a result of an underlying mental conflict most often during the unstable period of adolescence "most commonly in intelligent girls whose emotional constitution and autonomic nervous control are unstable" They state that there is no specific endocrine therapy for this condition and that reported responses to such medication is usually the result of its suggestive effect upon the hysterical nature Actually, permanent results are more likely if no artificial aids are employed

Differential diagnosis includes wasting diseases such as tuberculosis or malignancy Addison's disease is differentiated therefrom by its characteristic weakness, pigmentation, episodes of nausea and vomiting, and low blood sodium. In those conditions blood pressure may be low. In the addisonian syndrome there is no related fundamental psychologic disturbance and anorexia is not constant.

feature. Differentiation from Simmonds' disease (extreme insufficiency of the anterior lobe of the pituitary gland) is more difficult. Superficially the syndromes resemble each other, in both there is striking emaciation, amenorrhea, lowered basal metabolic rate, altered sugar tolerance, low temperature and psychological changes. By contrast, Simmonds' disease occurs more commonly in adult women who have had several children and who previously enjoyed good health. It may follow subsequent to a difficult labor which has been associated with some complication. Or it may follow invasion or destruction of the anterior pituitary lobe. Also there is absence of any preexisting psychoneurotic trend or of any precipitating emotional factor. The appearance of senility is more marked in Simmonds' disease and its amenorrhea is associated with loss of sexual function, of secondary sexual characteristics (loss of axillary and pubic hair; atrophy of the sexual organs). Furthermore the basal metabolic rate may be lower than in anorexia nervosa and because of the associated underfunction of the thyroid gland there may be response to thyroid medication, whereas in anorexia nervosa such response usually does not occur because the lowered basal metabolic rate is secondary to emaciation The blood sugar is usually lower and moderately severe anemia coexists, a rare finding in anorexia nervosa. The mental status In Simmonds' disease the is striking patient being dull and apathetic and showing gross changes in personality, while in anorexia nervosa the individual is generally quick, alert, restless, but may become "willful, sensitive, impulsive and hysterical" The characteristic pathologic change in Simmonds' disease is an almost complete destruction of the anterior lobe of the pituitary gland with secondary atrophic changes in other endocrine glands, viscera and skin.

Treatment—(1) The aim of treatment should be to change the attitude of the patient toward food; (2) eradication of the underlying mental conflict; (3) change of environment, encouragement, suggestion. Prolonged psychotherapy is often necessary before the patient fully understands the true nature of the illness which may be the offshoot of various environmental factors, past and present. Treatment in a hospital away from solicitous relatives is advisable, preferably in a public ward rather than in total isolation Frequent, small feedings of high Caloric value are advisable, and generous accompaniments of praise and encouragement In very advanced cases, feeding by duodenal tube may be necessary. The use of insulin and nonspecific endocrine therapy should be avoided. Occupational therapy is a valuable adiuvant.

Extensive psychiatric observations in 12 cases of anorexia nervosa are reported by L. Rahman, H. B. Richardson and H S Ripley⁵² and they regard this syndrome as a symptom complex occurring in a setting of psychoneurosis The underlying psychological mechanism seems to center around an unconscious repudiation of the patient's feminine rôle (all cases in this series were females) It is the opinion of these observers that "a neurosis serves as a protection against the assumption of normal sex relationships" Among the more important psychological trends reported are the fol-Marked reticence concerning sexual topics, strong repudiation of sexuality, the obsessive starvation serving as an excellent defense against the establishment of a love relation. In the unconscious of these individuals eating seems symbolic of impregnation and

obesity of pregnancy and both of these are subsequently avoided. All histories give evidence of poor heterosexual adjustment, only 2 of the women being married. Many cases have presented alternating periods of overeating and self starvation. Ascetic trends were common — the appearance of satisfaction derived from denying pleasures unto oneself. Obsessive and compulsive features were frequent—perfectionism, stubbornness, overconscientiousness, etc., as well as marked feelings of insecurity, high ambitions, extreme sensitiveness and seclusiveness. Many patients were very dependent and "good children." Almost all showed excessive physical activity. Social adjustment was poor At times there appeared to be a lively appetite but a compulsive abstinence Family histories of such patients frequently revealed neurotic disturbances in 1 or both parents (especially excessive attention to gastrointestinal function) serving as patterns of reaction for the child Many of the patients were obsessively addicted to purgatives. Over emotional dependence upon 1 parent was common, usually the mother. The more severe cases, in their earlier histories, showed a loss of weight from voluntary dieting in face of persistent appetite Such cases improved only with fairly deep psychotherapy. The milder cases almost invariably had shown a loss of weight following upon anxiety with its accompanying anorexia, in turn a response to some overt situation. These cases improved usually with intensive medical care without recourse being had to special psychotherapy. As these cases improved, ovarian function usually returned These authors again recall the hypothesis of the English school, to the effect that in anorexia nervosa the primary disturbance is emotional, "the pituitary blackout" of emotional origin.

RHEUMATOID ARTHRITIS

In order to establish whether there was a relation in time between the onset or exacerbation of arthritic symptoms and emotional or environmental crises, S. Cobb, W. Bauer, and I. Whiting⁵³ have studied a series of 50 patients with typical rheumatoid arthritis. The approach was from the medical, psychiatric, and social service points of view. This study points to a synchronism between social and medical events in the life histories of the majority of these patients, and the authors feel that their findings (checked with a controlled series of patients with varicose ulcers) point to the probability that such relationships represent more than mere coincidences. The types of environmental stress were principally in the form of poverty, grief and family worry

These investigators characterize rheumatoid arthritis as "a chronic disease of unknown etiology" In addition to articular involvement, usually symmetrical and more likely to affect the small joints first, these patients complain of constitutional, vasomotor, and neurologic symptoms, which may all precede the later skeletal involvement. Remissions and relanses are characteristic. The end result is often incapacitation. The many etiological theories that have been advanced are briefly reviewed, which include the infectious and neural theories. "Doubtless many of these erroneous theories represent failure to distinguish sharply between etiologic cause and contributing or precipitating factors"

ENVIRONMENTAL FACTORS IN PSYCHOSOMATIC RELATIONSHIPS

G. C. Robinson⁵⁴ has studied a series of 174 patients at the Johns Hopkins

Hospital in an effort to determine the "extent, nature, and significance of the disturbances of health caused by social factors" Adverse social conditions were found in 80 per cent of the cases, and in 56 per cent it was felt that the social conditions caused the emotional disturbances producing the symptoms.

C. P. Emerson⁵⁵ makes some pertinent remarks concerning the possible effect of so-called western "civilization" upon the incidence of certain diseases related to muscular spasm and hyperirritability of the autonomic nervous system. As the result of direct observations in some 300 hospitals in the Orient under western supervision, the striking absence of hyperthyroidism, angina pectoris and appendi-

citis, and other similar clinical pictures is emphasized. During this inspection of Oriental hospitals the author found "not a single case of acute appendicitis in nationals who observed their age-old customs and profoundly fatalistic religions."

This commentator recalls the frequency with which an individual in the western hemisphere will in his twenties be operated upon for appendicitis, in his thirties be treated for peptic ulcer, and in his forties have to submit to a cholecystectomy, meanwhile suffering much of the time from "colitis" The preceding affected organs are under the control of the autonomic nervous system and therefore in relationship with a mechanism involved in anxiety defense reactions.

SCHIZOPHRENIA

By Francis J Braceland, M.D., and Thurston D. Rivers, M.D.

Prevention—In any consideration of therapy of schizophrenia, it is important that several angles be kept in mind. First, perhaps the most important form of treatment of any disease is its prevention and schizophrenia is no exception to this. Secondly, if schizophrenia does develop, it calls for prompt and efficient treatment. Thirdly, the possibilities of remission decrease rapidly as the duration of the illness lengthens. Fourthly, and fortunately, the therapeutic weapons now at our disposal are more efficient than they have even been before

It has been estimated that every year approximately 30,000 to 40,000 individuals in the adolescent period of their lives fall victim to schizophrenia Puberty and adolescence present difficult problems which the personality must meet. Normally, it is a difficult period because of the physiological and psychological changes which are taking place in the

organism; therefore, it can readily be seen that if a maladjusted individual has been pyramiding his problems, the break which initiates the psychosis may occur at this time The specific causes of schizophrenia are unknown Adolf Meyer regards schizophrenia as a reaction type, the result of repeated failures of the individual to adapt to the environment. A long section view would reveal that the individual got off to a bad start and that instead of facing the problems which life presented he sought compromise and relief in fantasy life. Problems were met by means of roundabout methods, retreat into illness, neurotic complaints, suspiciousness, bizarre beliefs, and pathological reactions of various sorts

Obviously the time to begin prophylactic measures is early in the left of the child. The shy, retiring, seclusive, unsociable child should be the target of intense but careful psychotherapy. The

prime desideratum is the socialization of the child and efforts should be made to obtain a better adjustment between the growing personality and its environment. This, of course, can only be accomplished by judicious handling and any attempts to stimulate activity by shaming the child or using odious comparisons is liable to end disastrously. Finding the world unsympathetic such a child might retreat "into his shell" and secure his satisfaction by means of fantasy. The home, school and playground are the best places in which to carry out such prophylaxis. In all of them, intelligent understanding is an important requisite Harsh discipline or its opposites, spoiling and overindulgence is undesirable, as is dictatorship by bullies, childish, or adult. Companionship with other children of both sexes is desirable, and scholastic standing assumes secondary importance when the child's emotional life is in the balance. It is more desirable to have a normal, well balanced. none too brilliant citizen than a genius who requires confinement in a mental institution Sex instruction can be given safely at a comparatively early age, but it should only encompass degrees and details suitable to the child's age. The sexual problem is always a difficult one for the schizoid individual and therefore attempts should be made to supply proper knowledge of sex hygiene in a calin, unemotional manner in order to prevent retreat into fantasy and rumination

The parent-child relationship is most important, for in their weakness, the children buoy up their insecurity by identification with their parents. This bond, which ties the child to the parents or their surrogates, is a strong emotional one, and improper handling of it is a danger for an introverted individual. The goal of any real psychology of childhood is to obtain true emotional maturity

and the parent-child relationship must be slowly, carefully, and intelligently loosened before the final severance. In some instances, this separation is never completely accomplished, and it is often because of the parent's selfishness that the child is unable to make proper emotional adjustment.

Introverted children should be carefully and unobtrusively nurtured, most of them tend to get off alone and to read too much. The delving into abstruse subjects should be discouraged. They should not be allowed to choose vocations which are really only compensations for their inferiority feelings. Their life's work should be chosen with due regard for their various capacities, and in all instances they should be made capable of a normal social life on a broad scale

Treatment—If, in spite of prophylactic measures, the unfortunate individual does become schizophrenic, vigorous efforts should be made to combat the disease. It should be borne in mind that the patient's chances for recovery decrease in inverse proportion to the duration of the illness Procrastination is not permissible, once the definite diagnosis of schizophrenia has been made, proper treatment should be instituted

In most of the large clinics, insulin shock therapy remains the method of choice in a large percentage of schizophrenic cases. The 1939 reports of this type of treatment were optimistic for the most part. One thing seemed to stand out, and that was the necessity for a more widely accepted criterion for treatment. This has led us to discuss in detail the technic used in the insulin department of the Pennsylvania Hospital in Philadelphia

Insulin Technic—Contraindications
—1 A patient with physically demonstrable evidence of cardiovascular disease which would classify him as falling

under Class II or III, according to the criterion of the American Heart Association, should have an electrocardiogram and be more closely studied as to his functional capacity.

- 2. A case in which any evidence suggests the syndrome of hyperinsulinism should automatically be excluded from treatment.
- 3. Patients who have fever, amenorrhea of organic origin, or who show neurological evidence of organic lesion of the central nervous system should not receive treatment; those with metabolic diseases may be treated only after complete studies are made.

Actual Technic—The patient between 7:00 and 7:30 A. M is placed in bed and given the initial dose of insulin. This first dose is usually 15 units of U80 insulin. The first 6 injections are given by the physician in order that anaphylactic shock may be treated immediately. U80 insulin is used throughout the treatment and is administered intramuscularly into the deltoid muscle until the dose reaches large proportions, when it is given in the gluteus muscle

On the second day of treatment, the dose is increased if necessary, either by doubling or by increase of 10 units. according to the individual patient's reaction An attempt is made to have the patient receive a stupor dose between the fifth and eighth days of treatment An adequate stupor dose is 1 which will place the patient in stupor at 9.00 or 9.15 A. M. and maintain him in that state until 11 00 or 11:30 A. M., at which time he is aroused by the administration of glucose solution. Stupor may be said to begin when the patient loses actual contact with his surroundings either through mental confusion or sleep from which he cannot be roused. It continues through stages of hyperkinesia, somnolence, hypertonicity, etc , until terminated by coma or glucose administration. Our own use of the term coma denotes a state of complete areflexia: Corneal reflexes, the gag reflexes, the swallowing reflex, and even the Babinski reflex, which has been developed during stupor, are all lost. No attempt is made to induce this state as a routine procedure, and should the patient become comatose he is allowed to remain so only for 15 to 30 minutes.

Once a stupor dose of insulin has been reached it may be necessary to raise or lower it to keep the patient at a constant level, free from overexcitement or marked restlessness.

The dose of insulin required to produce stupor varies greatly. It is, of course, desirable to keep the insulin dose as low as possible for adequate treatment, but where large doses are required to produce stupor they must be used. Cases of prolonged coma and death from insulin would seem to bear no direct relationship to the size of the dose administered

It has been found that the combination of atropine sulfate, ½₁₅₀ grain (045 mg.) with the insulin injection is beneficial This reduces the amount of sweating, seems to diminish the early tremors, does away with hunger contractions of the bowel, nausea due to gastric secretion, and pylorospasm, as well as reducing pulmonary secretions. The fact that it increases the heart rate slightly and may cause mydriasis must be borne in mind

Convulsions in the later stages of stupor are not considered harmful unless there is some physical contraindication, and in certain cases they have been found helpful. Convulsions cannot be induced at will and neither can they always be prevented. A strenuous attempt to avoid them usually results in poor stupor and inadequate treatment. Convulsions in the early stages of stupor, on the other hand,

are undesirable, since the patient must be given glucose within 15 minutes after the convulsion is over, and the stupor period is thus shortened. On the day following a convulsion, the insulin dose is changed to avoid a second one. It is interesting to note that the same dose which produced a convulsion, if repeated at a later date, will very frequently not result in a convulsion

Between 11:00 and 11:30, glucose solution is administered to those patients on the maintenance dose This allows 2 to 2.5 hours of stupor. If the patient has not reached the stupor stage, he is given 33 per cent oral glucose solution flavored with orange or lemon juice to which has been added 1 gram of sodium chloride. One ounce of this solution for each 5 units of insulin is the usual ratio. Breakfast is then served and the patient is allowed to return to the ward. To those patients who have reached the stupor stage, 50 cc of 25 per cent glucose solution are administered intravenously. The reaction should be evident in 5 or 10 minutes, but if necessary another 50 cc are given immediately. Oral glucose is then given, followed by breakfast Where the dose of insulm is so large as to require the administration of excessive amounts of glucose-orange juice solution to maintain the ratio mentioned, nausea may result. In such cases, the amount is reduced and the ward is advised to supplement it with glucose during the afternoon

The length of treatment is determined by the progress of the patient. Early improvement does not necessarily mean that the course of treatment may be shortened, except in unusual cases the patient should receive a minimum of 40 treatments Cases demonstrating a favorable reaction late in the treatment should have a prolonged course of 60 to 70 treatment days. Those who have a late

stupor reaction may require longer treatment than patients with early stupor.

Psychotherapy accompanies insulin treatment in the unit in the forenoon and on the ward in the afternoon. If possible, it should be understood by the family that the patient should remain in the hospital for 2 to 4 weeks after cessation of insulin therapy in order to assure an adequate readjustment and to diminish the possibility of relapse.

From a statistical standpoint, Ross's 56 study of 1356 schizophrenic patients from the New York Hospital System was of the greatest importance. All of these patients had been treated with some drastic form of therapy. In evaluating the results of the treatment, Ross laid down the following criteria. In order to classify a patient as "recovered," the individual must be symptom free and must have insight into his illness. By "insight" he means that the patient must fully realize that he had suffered a mental illness and that his symptoms were part of his illness. He must also be willing and able to speak of his illness objectively and in detail with normal effect. He must also be able to adjust well in the community on his prepsychotic level The term "much improved" signifies that the patient is symptom free but insight as defined above is lacking or incomplete although he is able to adjust well in the community at or near his prepsychotic The patient is considered "improved" if his symptoms, while not completely alleviated, are less distressing and he is able to make a better adjustment than before treatment "Unimproved" means that the patient has received no benefit from the treatment. The above criteria eliminate the personal element insofar as is possible. Based on these dicta, 142 per cent of the 1356 patients recovered, 206 per cent were much improved, 26 3 per cent were improved, and

38.9 per cent showed no response to the insulin shock. In over half of the cases the illness had been of 2 or more years' duration. From his statistics, he drew the following conclusions:

- 1. Beneficial results from treatment of all cases of dementia praecox under insulin therapy, no matter how long the duration of the illness were much better than in the untreated groups
- 2 The results following treatment with insulin are much better than results following metrazol therapy alone
- 3. Combinations of metrazol and insulin apparently act in selected cases.
- 4. The results obtained in cases of over 2 years' duration not only justify the time and expense but demonstrate that it would be an error to neglect such cases
- 5 Recovery and improvement rates are progressively smaller the longer the duration of the illness
- 6 The dangers of drastic therapy in the hands of the trained physician are almost negligible
- 7. An active educational campaign should be carried on so that early diagnosis of dementia praecox will be made and treatment instituted at the earliest possible date

Niver, et al, 57 report 106 cases with a total and social remission in 32.07 per cent. As to the type of schizophrenia benefiting most frequently from insulin therapy, the same authors feel that the paranoid type offers the best possibilities, the catatonic next best, and the hebephrenic type a poor third The authors also state that cases with total remissions are in little danger of relapsing, whereas those with social remissions are in considerable danger if they are discharged too soon from the hospital Bowman, Wortis, Fingert and Kogan⁵⁸ conclude that relapses do occur after successful insulin treatment, but they believe then to be due to shortcomings in the technic of administration They feel that these relapses are readily amenable to a second course of treatment Young and Young 59 fail to find a common cause for relapses but they feel that the less complete the remission, the greater the tendency for reappearance of the psychotic picture.

Reports of insulin treatment which emanate from South America⁶⁰ are even more enthusiastic than those of our own country. They seem more nearly to approximate the European reports which in general are higher than those reported by American workers.

Insulin and Metrazol (Combined)

—The combination of insulin and metrazol therapies in the treatment of schizophrenia has met with favor in this country, particularly in selected cases. It was first suggested in the United States by F. Georgi and R. Strauss.⁶¹ The technic as described by Ruslander⁶² begins with the production of insulin coma in the orthodox fashion, but near the end of the period of stupor a metrazol convulsion is produced. Nine cases who had failed to respond to insulin therapy alone were reported by Ruslander. Three of them were definitely improved, 1 to such a degree as to warrant parole Reese⁶³ feels that this offers a valuable adjunct to therapy, particularly in the catatomic type of schizophrenia. It should be emphasized that this is a combination of insulin and metrazol therapy—it is not the use of insulin in the subordinate rôle of allaying the fear incident to the metrazol convulsion or lowering the metrazol convulsive threshold as advocated by Sands 64

Malamud and Gottlieb⁶⁵ point out that the results of insulin shock therapy must be analyzed objectively and without prejudice in order to avoid over enthusiasm or unjustified censure. Therapeutic efforts against insulin were used before the advent of Sakel's treatment. They state that results obtained in schizophrenia with the psychotherapeutic method are the most valid basis of comparison with shock therapy.

Taking the reports of the New York State Hospital service on shock therapy (1879 cases), those of Cheney and Drewey (142 cases) and of Malamud and Reuder (177 cases) on psychotherapy, "it may be said that in general patients treated psychotherapeutically have fared probably as well as those treated with insulin while those treated with metrazol show a much lower percentage of good results."

Metrazol—In the literature of the latter part of 1939, the trend seems to be away from the use of metrazol alone as a treatment for schizophrenia Steinberg, et al.,66 report on 300 cases treated with metrazol with a 37 per cent "amelioration" of symptoms They found that in the chronic group metrazol gave better results than insulin therapy but that insulin therapy used in patients ill less than 18 months showed a higher remission rate than a similar group treated with metrazol. Bookhammer and Plesset⁶⁷ report on 87 schizophrenics treated with metrazol Eight per cent showed complete remissions, 8 per cent made a social recovery, and 10 per cent were improved, thus leaving 74 per cent unimproved. They also add that of the 14 patients who were greatly improved by treatment, 12 had been ill less than 1 year The type of schizophrenia responding best to metrazol therapy in their group was the catatonic (both excited and stuporous), the paranoid group to a lesser degree They feel that "the response of patients with schizophrenia to this treatment has not exceeded the expected rate of recovery of persons not receiving such treatment" Ross⁶⁸ reports 1140 schizophrenics treated with metrazol He concludes that "Metrazol . . . produced even fewer recovered cases than those not treated by any shock therapy." He feels rather definitely that its use in schizophrenia should be

confined to a combination with insulin such as we have already described.

Shapiro and Freeman⁶⁹ in a report on 300 schizophrenics treated with metrazol record their results according to duration of illness

Group I—19 patients ill for less than 6 months. Eight or 42 per cent made a complete remission; 6 or 31 per cent made a social remission; a total of 73 per cent total and social remissions in this group.

Group II—46 patients ill from 7 to 18 months Ten or 22 per cent made a total remission; 7 or 15 per cent made a social remission, a total of 37 per cent total and social remissions in this group.

Group III—146 cases ill from 19 months to 5 years. Eleven or 7.6 per cent made a total remission, 6 or 41 per cent made a social remission; a total of 117 per cent remission rate

Group IV—89 patients ill over 5 years No total or social remissions obtained

In comparing their results from metrazol alone with a smaller group treated with insulin, they conclude that "insulin therapy in patients ill less than 18 months shows a higher remission rate than a similar group treated with metrazol.

It has been our own impression that the group responding most favorably to metrazol are the young patients with an acute catatonic episode of short duration Cases of longer duration may be improved from the standpoint of hospital management but can rarely be considered even social remissions.

The first report in America by Bennett and Fitzpatrick⁷⁰ on fractures produced by metrazol has resulted in more careful consideration in selecting the cases. In 17 patients treated, they found that 47 per cent suffered compressed fractures of the vertebral spine. All these fractures occurred in the dorsal spine and none was disabling. Rupp⁷¹ reports dorsal spine fractures in 13 of 36 cases treated. He feels that many of these fractures were due to the unlimited movements allowed the patient during

convulsions. In 687 cases treated with metrazol in the New York Hospital System, Carp⁷² found 1.78 per cent fractures and 172 per cent dislocations. Of the series of fractures, 5 were of the neck of the femur, 1 fracture of the greater and lesser tuberosity of the humerus, 1 fracture of the anatomic neck of the humerus and greater tuberosity, 1 fracture of the angle of the mandible, 1 fracture of the seventh thoracic vertebra, 1 fracture of the transverse process of the fifth lumbar vertebra, and 2 fractures of the greater tuberosity of the humerus. This percentage of fractures with the extremely low number of vertebral injuries would seem out of keeping with the observations of others. Our own observations seem to be in agreement with the more recent estimates of about 10 per cent fractures of dorsal spine, and 1 per cent miscellaneous fractures

Azoman—There is a rapidly accumulating literature on the use of triazol or azoman (cyclohexyl-ethyl-triazol) Napier⁷³ reports from England that he believes this convulsant is an improvement on metrazol in all psychoses in which convulsive therapy is of value. Its dose is smaller, it may be administered orally, parenterally, or intravenously, it may be slowly injected, and there is less objection on the part of the patient to this treatment. The use of this drug by Hoven⁷⁴ would seem to indicate that its value in schizophrenia is about the same as metrazol

Convulsive Therapy by Means of Electrical Shock—In 1934, Cerletti⁷⁵ employed an alternating current of 125 volts to produce experimental convulsions in dogs. After the standardization of convulsive treatment, the method was modified for human beings. The apparatus consists of a timer, capable of regulating the length of shock over fractions of a second and a means of

measuring and graduating the current. A supplementary apparatus measures the resistance of the subject's lead by means of a minute current. The electrodes are applied by means of a special band. A current of 300 to 600 villiamperes at a strength of 8 to 115 volts, applied for 5 to 7/10 seconds, is ordinarily used. When the current is applied, the patient immediately loses consciousness without signs of distress and there develops a generalized tonic spasm. This is followed by pallor and then cyanosis; respiration is arrested for a moment. After about 30 seconds the color returns and a typical generalized convulsion occurs, lasting about 2 minutes. The pulse rate is little affected. Consciousness is regained in 8 to 10 minutes and the patient has no memory of what has occurred. The attack may be repeated immediately if desired The method has not yet been used in a sufficient number of cases to justify an opinion as to its therapeutic The results have so far been good, and there is every reason to believe that they should at least equal those produced by other convulsants, with less danger. No publications concerning this type of therapy have appeared in this country.

Kolinowsky reported in the December Lancet that "to date several thousand fits have been produced on some hundred patients, partly in the Rome Clinic and partly in other institutions without any accident whatever" The effects of the shock on the brain are not yet completely worked out. Accorners is now working on histological changes after electric shock In a personal communication, he states that even with much higher voltage than used in man, animals show only unimportant and reversible changes.

Nitrogen Therapy — Based on the original work of Himwich stating that the beneficial results of metrazol and

insulin therapy probably depended upon the cerebral anoxemia, and based upon a modification of the Albany technic, Ruth, Flaherty. Pearson and Smith⁷⁶ report on 20 cases treated with nitrogen therapy. Fifteen of the cases treated were schizophrenic and of this number, 4 had remissions. In a study of these 4 remissions it was found that 2 had had previous psychotic episodes from which they had recovered without treatment A third recovered case relapsed after 6 months spent in her former environment This leaves only 1 case of the 15 recovered, a remission rate not out of keeping with spontaneous remissions. Of the 15 cases which failed to respond to nitrogen therapy, 9 received insulin or metrazol therapy. Of this subgroup of 9, 5 gained full remissions, 2 made recoveries with slight defect. These authors further conclude that "in the pharmacological treatment of functional psychoses, the rôle of cerebral anoxia as the important effector of recovery is questionable"

Total Push Method - The "total push" method was first outlined by Abraham Myerson,77 and is based upon the theory that "schizophrenia is, in certain of its characteristic manifestations, a retreat from social contact into delusion -such a patient is placed in an institution—the physiologic retreat of the schizophrenic is enhanced in all directions by the usual hospital care which he receives " He feels that a change in the activity of 1 group of functions may restore or assist in restoring the activity of the organism as a whole The "partial push" which he describes is the use of hydrotherapy, physiotherapy, the use of drugs, diet and exercise, as well as occupation and entertainment Total push is based upon the following measures.

General Medical Measures-

1. Physiotherapy "The value of showers, douches, massage and rubdowns to give first

- a start to the patient's energies and, second, because of their general tonic effect."
- 2. Irradiation ultraviolet irradiation is thought by the author to increase the hormone activity of the patient and he therefore incorporates it in his Total Push.
- 3. Exercise and Games. One of the essential difficulties in these patients is the inertia and even resistance of the patients to games and exercises Passive motion is used where active participation in a game cannot be achieved at first "Our experience has been that in a relatively short time the patients cooperate in games of all kinds, go through exercise with vigor and with considerable skill in a manner quite surprising in view of their general mertia on the wards"
- 4 Diet and Vitamins—"An increased and more liberal diet with eating in common with the others." Vitamins in their various combinations are used without the actual clinical evidence of their deficiency.
- 5 "Psychological Push" Clothing—particular attention is given to the awakening of a consciousness in appearance "One of the sources of a human being's egotism is his clothing. One of the principal entries of normal human relationship is in what men wear (and particularly in what women wear)"

Praise, Blame, Reward, Punishment—
"Praise and blame have not been used so much as reward and punishment. Reward in the form of more privileges, candy, ice cream and the retention of the added foodstuffs, delicacies, cigarettes, cigars—the giving and taking away of these rewards and punishments has constituted the main motives up to the present time." The author feels these factors are an important part of the method. Education, though not as fully described, is thought to be a valuable part of the method as the patient advances.

Results in the total push method are described by Tillotson.⁷⁸ "Eleven deteriorated patients suffering from chronic schizophrenia, who have been ill for an average of 12.1 years . . . have been treated 3 months with the total push

method; 22 patients have been treated a shorter period of time. All of the 33 patients showed slight improvement. In none of these patients has the condition become worse."

Tillotson offers the suggestion "... if insulin and metrazol therapy are used, the total push method should be instituted in its fullest sense as an important adjunct."

MANIC-DEPRESSIVE PSYCHOSIS

By James A. Flaherty, M.D.

Alterations in the Fundamental Concept — The nosological grouping, manic-depressive psychosis, has been used in a very decisive way, carrying with it the inference of a definite prognosis Recovery is assumed and the question seems only one of duration of the episode, and of subsequent attacks. The clinician is confident of a benign, even if repetitive course The essential fallacy of this conception is stressed by Aubrey Lewis 79 He feels it best to think of a wide range of affective psychoses, with an extreme group, in which constitutional factors are vastly more important than environmental ones; and milder affective states, readily responsive to situational factors, mostly with depression and anxiety, and with a general drift toward chronicity

Leslie B Homan⁸⁰ in a 7-year followup of a series of 144 cases, comments that only one-thirteenth showed elation, and further remarks that he cannot beheve that we are looking at the same illness in all affective disorders. He feels it wise to abandon the classical descriptive categories, since they contribute so little to prognosis and therapeusis Reenforcing this attitude is the discussion by Bertram D. Lewin,81 who calls attention to a neurotic type of hypomanic reaction He differentiates the true hypomanic picture from the neurotic one by the fact that the latter does not make the extensive use of the mechanism of denial employed by the true hypomanic. He feels that the neurotic type represses or uses a compulsive-obsessive reaction to deal with unwelcome psychological material. He believes the mechanism of identification is important in both types Dupouy and Barret⁸² call attention to the emotional fugue states of a psycho-neurotic character which are recurrent.

Increasingly accepted is the separation of involutional melancholia from the manic-depressive psychoses. Hoch and McCurdy's constitutional and personality conceptions have been widely corroborated, and emphasized most recently by the studies of H D. Palmer and Steven S Sherman (Personal communication)

Robert C Hunt and Kenneth E. Appel⁸³ in a study of reaction types with an almost equal admixture of schizoid and cycloid symptoms, present evidence that these represent a group affording clearer clinical understanding and distinctive prognosis Of the 30 cases which they collected during the years 1919 to 1929, and have followed to date, a recovery rate of 36.7 per cent was observed, while 333 per cent were unrecovered, never attaining a remission authors remark, therefore, that the recovery rate in schizomania, so-called, is roughly twice as great as in schizophrenia (in the absence of insulin therapy), and from 25 to 50 per cent lower than that found in the true manic-depressive psychosis

Heredity—Elliot Slater⁸⁴ presents an illuminating study of 3000 cases of manic-depressive psychosis studied in Kraepelin's Clinic in Munich Employing careful diagnostic criteria and excluding cases presenting schizophrenic features, he was able to obtain a group of only 72 pure manic-depressive cases. A second group of 68 was also studied. These, however, were featured by exaggerated hypochondriasis, intense irritability, and/or a basic paranoid personality matrix. He feels that the previous work on the inheritance of manic-depressive psychosis has failed to meet the strict requirements demanded in genetics. He concludes that there is no single gene responsible for the condition known as the manic-depressive constitution commenting on the importance of the genotypic milieu, he remarks that any single quality is probably contingent not upon a single gene, but rather on the totality of genes He concludes that even though 1 gene were responsible for the deviation, the degree to which it would become manifest is governed by a variety of circumstances, genetic, environmental and confusional (exogenous)

Lewis, commenting on genetic prognosis, finds maximum inheritance where both parents exhibit clinical manic-depressive episodes, or where 1 parent is definitely manic-depressive while the other is melancholic, sanguine or cyclothymic. Where 1 parent is normal and the other manic-depressive, one-third of the siblings show the disorder

Etiology—L. J. Karnosh and J M. Hope⁸⁵ in a study of puerperal psychoses and their sequelae, present interesting data on women of cyclothymic disposition who developed an affective psychosis following childbirth. The various deliria with affective changes occurring during the lactation period eventuated in subsequent manic-depressive attacks,

to which the patients had not before been subject. The authors feel that the toxicaffective illnesses induce an organic change, which thereafter expresses itself in the form of a more exaggerated cyclothymic disposition. This organic conception when juxtaposed with that of James W. Papez⁸⁶ concerning the mechanism of emotion, should encourage illuminating speculation and study

Stockings⁸⁷ recently reported upon his study of mescaline psychosis. Although the toxic psychotic state so produced is condensed and endures for a matter of but a few hours, the pattern of manifestations suggests a confusional picture, a dissociated schizophrenic illness, and an affective disorder. He calls attention to the patient often seen in hospital practice who presents an early acute confusional state which is followed by a typical picture of mania, later changing to a true schizophrenic illness. On this basis he is of the opinion that there is strong evidence to suggest that all the various disease processes described as functional psychoses have a unity of origin makes the interesting assumption that the psychoses, excluding the organic ones, are all variants of the same disease process and that the causative agent is a toxic body with chemical and pharmacological properties similar to those of mescaline

Prognosis—Lewis feels that the outlook for complete recovery is good in an individual with a manic-depressive episode, where a solitary or periodic, but typical affective illness occurred in only 1 parent. He suggests doubt as to eventual outlook in cases in which eccentric, neurotic or schizophrenic antecedents are predominant. In syntonic individuals with pyknic habitus, who undergo uncomplicated attacks, the return to health is more likely than in individuals in whom schizoid or other

psychopathic personality factors enter the picture. He calls attention to the fact that the patient who prepsychotically presents morbid traits, i.e., who is anxious, frictional, suspicious, odd. solitary or obsessional, undergoes no magic alchemy of the personality through an affective explosion; on the other hand, recovery from such an episode may be long drawn out. Earl D. Bond and F. J. Braceland⁸⁸ in a follow-up of 171 manicdepressives admitted for hospital care in 1927-1928, found 86 of this group recovered. The total of 171 represented 24 per cent of the admissions to the Pennsylvania Hospital in 1927-1928, and contrasted curiously with the figure of 15 per cent, or 11 manic-depressives out of 735 total admissions in a comparable period at Burgholzli Anstalt in Switzerland. This is of particular interest from the standpoint of geographic incidence, if the difference in diagnostic criteria is not too broad Of 8000 cases of manicdepressive psychoses in the New York State hospitals between 1910 and 1919, the Commission statistician, reporting to Dr Adolph Meyer, states that 50 per cent of first attacks, 25 per cent of second attacks and 10 per cent of third attacks were permanently well

Therapy—Although the major emphasis of hypoglycemic and convulsive therapy has been directed to dementia praecox, the extra-schizophremic application of these methods has received considerable attention. Insulin therapy has been found to contract the duration of attacks of manic-depressive depressions and has been reported to have an ameliorating effect upon the manic phase of the psychosis Strecker, Alpers, Flaherty and Hughes⁸⁹ report favorable results in the manic phase with convulsive therapy Singer⁹⁰ has reported very favorable results metrazol in manic attacks and contrasts its greater effectiveness with narcosis therapy. Bennett⁹¹ observed encouraging results in the older age group, whose agitated and depressive symptoms had not responded to hematoporphyrin, fever therapy, narcosis or appropriate endocrine treatment. Menninger⁹² reports his belief that convulsive therapy may be more effectual in depressions than in schizophrenia.

Injury of the thoracic spine incident to metrazol convulsions has not been sufficiently studied to evaluate its remote sequelae. It should be considered as a possible complication, however, when this form of therapy is elected. Recent observations have shown compression fractures in a high percentage of cases. Paradoxically, the most severe roent-genological damage is often clinically asymptomatic. No neurological damage is reported.

Efforts have been made to find analeptic agents which would be less severe in their effect upon the patient than Picrotoxin, coriamyrtin, metrazol ammonium chloride and azoman have been used with varying degrees of success Bennett has approached the problem from a different standpoint and has used curare intravenously to decrease the severity of the convulsion This approach is of great interest insofar as it serves successfully to eliminate most of the mechanical dangers inherent in a However, extreme caution convulsion should be employed in the use of the method, since the pharmacological effect of numerous alkaloids contained in curare upon human tissue has not been thoroughly studied Curarine is known to have a specific toxic effect upon heart muscle

The use of the nitrogen inhalation method of Himwich, 93 Alexander and Leipetz has not proven to be of clinical value in the treatment of manic-depres-

sive episodes. However, it does continue to be an extremely important investigative method.

H. Tomasson⁹⁴ used *ephedrine* and *acetylcholine* with some small encouragement from the results. *Benzedrine* has been used with modest success in the mild cyclothymic depressions, and depressed states of which the core is essentially psychoneurotic. J. Loman, A. Meyerson, W. Dameshek and E. Guttmann⁹⁵ have made interesting reports on the use of this new sympathomimetic drug in psychiatric practice

T. J Hennelly 96 successfully employed prolonged narcosis with somnifen, while D. Palmer and F. J Braceland,97 reporting on 6 years' experience with sodium amytal narcosis, feel that it is a valuable instrument, the most dramatic use of which is in the acute manic attack These authors reported a series of 100 treated cases. Of these, 32 were manic episodes, 60 per cent of which had an immediate remission, while 27.5 per cent showed permanent or temporary ability to maintain a higher level of social adjustment following narcosis treatment E A Strecker, H D Palmer and F J Braceland98 used synthetic hematoporphyrin hydrochloride 111 cases of manic-depressive depression, and observed improvement in 364 per cent. with moderate improvement in 182 per cent

Harold A Palmer, of Woodside Hospital, London, published the most comprehensive review of narcosis therapy in mental disorder yet to appear in the literature. He feels that the useful therapeutic effect of narcosis is related to the narcotic effect upon (a) the cortex, (b) the subcortical region, (c) the cortical-subcortical region, (d) the sudden withdrawal of sedatives after their prolonged use, (e) the specific

barbiturate effect, (f) the facilitation of psychotherapy during sleep.

He enumerates and analyzes the different methods employed, such as that of Klasi, MacLeod, Wolff, Withold and Meerloo. He also briefly discusses Cloetal and its use at Zurich. He investigated the recovery rate in manic-depressive psychosis, schizophrenia, anxiety states and alcoholism with narcotherapy. He has also compared the response of the Kretschmerian types of habitus to narcosis, finding the pyknic type to be most benefited

He feels that factors bearing on recovery, utilizing this therapeutic instrument, are (a) the duration of the psychotic episode, (b) the age of the patient, (c) the amount of sleep secured and (d) the presence or absence of complications peculiar to the treatment.

In addition, he quotes Muller, who has collected to date all the mortality figures since 1925, which is 5 per cent. He discusses the mode of action of narcosis and evaluates its usefulness as a therapeutic method in the pychoses briefly as follows. (a) In a mixed series of cases it yields 33½ per cent recoveries. The recoveries occur especially in psychotic episodes which otherwise have a good prognosis (b) These recoveries are due to treatment (c) Since there is a 5 per cent mortality rate, the risk should be anticipated by scrupulously careful nursing (d) The effect of treatment is due probably to both somatic and psychological factors

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RESPIRATORY TRACT, DISEASES OF

By Frank Walton Burge, M.D.

BRONCHIECTASIS

Prognosis—A T Edwards¹ believes that although bronchiectasis is now considered to be a progressive disease, sufficient evidence to provide undoubted proof of this is lacking. By investigation it may be possible to prove that certain types of bronchiectasis are progressive, whereas other types may remain stationary for long periods, or even retrogress.

It is definitely recognized that in bronchiectasis following prolonged retention of a foreign body which has subsequently been coughed up or removed, or following the obstruction caused by a benign tumor which after removal has left no narrowing of the bronchial lumen, the disease often becomes progressively worse.

Such proof as is obtainable points to the fact that bronchiectasis in children

and adults is a progressive disease which in a large proportion of cases ends fatally.

Treatment—A T. Edwards¹ states that the medical care of bronchiectasis until quite recently consisted of the use of expectorants, the administration of creosote by mouth, and the treatment of complications, such as recurrent attacks of pneumonia and hemorrhage, by bed rest and careful nursing. Recently, however, considerable benefit has been derived from postural drainage. Many patients with widespread bronchiectasis can be kept relatively comfortable, and may lose the fetor often associated with the disease by postural drainage for onehalf hour mornings and evenings. Artificial pneumothorax has been advocated, but must be considered unsatisfactory in established bronchiectasis.

The object of *phrenicectomy* and *thoracoplasty* is to keep the cavities empty and to prevent the retention of secretion by compression of the lung. In some cases, paralysis of the diaphragm results in improvement, probably as a result of the alteration in the direction of the basal bronchi from a vertical to a horizontal position by the rise in the diaphragm

Thoracoplasty has resulted in great improvement in many cases of unilateral bronchiectasis, but if the disease is localized, the pulmonary collapse produced by the operation often occurs at the expense of the relatively normal tissue

Lobectomy—A T Edwards¹ states that excepting the risks of the operation itself, all the complications of lobectomy occur as the result of sepsis They include suppurative pneumonitis, secondary hemorrhage, cerebral abscess, and suppurative pericarditis

Any procedure which permits the safe creation of firm adhesions between the unaffected portion of lung and chest wall will greatly serve to reduce the mortality of lobectomy, by the double benefit of a minimum of pleural cavity to be infected and a minimal amount of respiratory disturbance during and after the operation. The prevention of extensive pleural infection is most important in lobectomy.

The indications for lobectomy may be summed up by stating that bronchiectatic patients between the ages of 4 and 40 years, in whom the disease is reasonably localized and infected, and in whom there is no serious general contraindication, should be considered as candidates for radical excision of the portion of lung affected

Lobectomy and pneumonectomy provide the greatest advance in the treatment of bronchiectasis. They are procedures which are associated with a mor-

tality that should be negligible if the disease is treated in its early stages, and which have a high proportion of curative results.

F. Sauerbruch² influenced by statistics from more than 500 clinics, hospitals and sanatoria in Germany and elsewhere, believes that surgery is an important treatment in traumatic bronchiectasis, contraction bronchiectasis and congenital dilatation resulting from malformations of the bronchial branches.

The unilateral lobectomy of the Munich Clinic was abandoned because of retraction of the bronchus stump into the mediastinum and a multiple-stage extrapleural technic developed

Brunn has revived the 1-stage lobectomy, but he uses a different technic. An important advance is drainage of the chest cavity One-stage lobectomy is indicated chiefly in younger individuals with localized findings. The 2-stage procedure is safer and easier on the patient

An in-between method is that of Nissen. Packing and drainage are included in the armamentarium of surgical therapeutic methods.

The present plan of lobectomy, according to I Sebestvèn, calls for a preliminary induction of phrenic paralysis. At the first thoracic operation, the seventh to ninth ribs with the intercostal tissues are resected for a distance of 11 cm back to the transverse processes. If the pleural space is found to be obliterated, the extrapleural mobilization of the lobe can be done at this stage. However, if the pleural space is found to be still open, as is usually true, its closure must be brought about by the formation of adhesions. At this first stage the costal pleura is separated as far as possible from the chest wall and a pack of petrolatum gauze inserted to stimulate the formation of adhesions between the visceral

and parietal pleurae. The wound is closed except for the lower angle.

Three or 4 weeks later the next stage is performed. In this and subsequent stages, the lobe is completely mobilized, the separation being started along the diaphragmatic portion. When this mobilization has been accomplished, the hilus is ligated with a rubber catheter and the necrotic lobe removed with a cautery 3 or 4 days later. The wound is packed open and allowed to heal by granulation with the constant development of a bronchial fistula

After partial filling in of the thoracic wound, the bronchial fistula is closed by means of a muscle pedicled graft. The usual time required for complete healing is from 4 to 4½ months.

A. T Edwards¹ reports that a satisfactory way to obtain adhesions is to blow B. P. C talc powder (magnesium silicate to which 0.5 per cent iodine has been added) onto the unaffected lobe of the lung, which is collapsed by a previous artificial pneumothorax. The air which is introduced into the pleura before operation is immediately withdrawn and the cannula is removed. This procedure (pleural poudrage) is carried out under local anesthesia. Firm adhesions develop within from 3 to 6 weeks. There appears to be no deleterious effect on the lung itself.

BRONCHUS

Diagnosis—Bronchography in Children—C. W. Lester and E A. Rovenstine³ report a substitute method for local anesthesia employed in bronchography in conscious children. The technic is one of inhalation anesthesia with nitrous oxide-oxygen, after basal narcosis with tribromethanol in amylene hydrate and the application of a 3 per cent solution of metycaine to the mucous

membranes. The method permits the accurate introduction of the contrast medium by way of an endotracheal tube and the removal of most of it after the bronchographic examination is completed.

Results after more than 1 year's trial indicate that the method is relatively safe, pleasant for the patients and time saving, and also that the results have been more satisfactory than with any other technic used.

Nephrobronchial Fistula

Diagnosis — H. P. Lee⁴ states that bronchial fistula should be suspected in those cases in which the patient gives a history suggesting a pathological process in the kidney or perinephric abscess, accompanied or followed by pulmonary symptoms, severe cough, and profuse sputum

Some degree of pulmonary involvement probably accompanies many perinephric abscesses, but the sudden onset of severe cough and profuse purulent sputum is a particularly significant symptom of bronchial involvement. Physical findings suggesting perinephritic abscess, râles or dullness in the overlying lung base, and elevation of the diaphragm with an overlying inflammatory process in the lung (as shown by x-ray films) may give additional evidence.

Cystoscopy and pyelography may reveal nothing, or one may find pyone-phrosis with escape of the pyelographic medium into the perirenal area, occasionally the patient may taste or even expectorate the pyelographic medium. Rarely can the nephrobronchial tract be visualized with x-rays.

Treatment—Drainage of the perinephric abscess usually results in immediate and marked relief of the cough and sputum, with a more gradual but usually complete clearing up of the pulmonary involvement. When the kidney

is markedly involved, *nephrectomy* may be necessary later.

Inflammatory Bronchial Stenosis and Bronchiectasis

Treatment — P. H. Holinger⁵ states that inflammatory bronchial stenosis which produces complete or partial bronchial obstruction leads eventually to atelectasis and then to bronchiectasis. Such cases recognized early and treated bronchoscopically result in clearing of the original lesion and the process is aborted.

Inflammatory bronchial stenosis has been found to be responsible for the production of the original pulmonary lesion, atelectasis. "Atelectasis precedes and plays a prominent and most constant rôle in the development of a common form of bronchiectasis of the lower lobes" (Anspach, 1934). Persistent pulmonary changes simulating pneumonia are frequently due to atelectasis. If the lung does not clear spontaneously, early and frequent bronchoscopic drainage of the involved bronchi will prevent permanent dilatation and destruction of the bronchial walls, which follow if the atelectasis is left untreated

LUNGS

Atelectasis

Treatment—A. E. Moore⁶ states that in the surgical service of the Cincinnati General Hospital any patient developing a sudden or unexpected elevation of temperature or respiratory rate during the first 2 postoperative days is suspected of having atelectasis until proved otherwise. If a diagnosis is established, the following procedure is carried out:

If not already in use, a tight abdominal binder is applied The patient is changed from Fowler's position to one in which the pillow is removed and the head is dropped flat, leaving the knees elevated. A chair is placed under the foot of the bed and the patient is turned so that his affected side will be up. The physician then stands behind the patient and places 1 hand on the uppermost shoulder, rolling the patient slightly forward on his abdomen. This puts the main bronchus in a true vertical position and secures the greatest gravitational effect on the bronchial secretions. The patient is instructed to place his uppermost hand on his abdomen, over his wound, and this is reinforced by the free hand of the physician. Occasionally, simply placing the patient in this position initiates violent coughing, but if coughing is not forthcoming the patient should be encouraged to cough.

In the majority of cases, the mucous plug will be loosened by the first guarded cough and an uncontrollable cough reflex set up with the production of a sizable quantity of mucus Coughing is encouraged until rhonchi no longer can be felt by the palpating hand. It is not uncommon for such a patient to volunteer the information "that's all."

If this fails or if the patient refuses to cough because of incisional pain, further efforts are aimed at loosening the plug. He is asked to take a few deep breaths If this fails to produce the plug, a sharp blow on the back will often accomplish the desired result. If these maneuvers fail, inhalations of carbon dioxide are given to increase the depth of respirations and this will frequently loosen the plug. If rhonchi still persist and breath sounds are not coming through the involved lung, the patient is forced to remain in the described position for as long as half an hour at a time. During this period steam inhalation of tincture of benzoin is given. The steam thins out the mucus, and the gravitational effect is enhanced by being allowed to act over a

period of time. This entire regimen is not used frequently, as the obstructing mucous plug ordinarily can be produced by simple forced coughing.

The foregoing type of postural drainage has given marked uniformity of success in relieving postoperative atelectasis. The most striking relief has occurred in those cases in which the atelectasis is recognized within an hour or 2 after onset.

Carcinoma

Etiology—F. H Muller⁷ states that considerable increase of primary carcinoma of the lungs has been observed in the recent decades. The exogenic character of the causes seems to be increased street dust, exhaust gases of motor cars, tarring of the streets, war gases, x-rays, trauma, influenza, tuberculosis, and increasing industrialization.

The simultaneous increase of carcinoma of the lungs and consumption of tobacco supports the view lately that smoking is a primary cause of carcinoma The tar content of tobacco is due mainly to the lignified parts of the leaves, such as the veins, and, recently, these have been used in increased quantities in the manufacture of tobacco. The cancerigenic effect of tobacco tar has been demonstrated experimentally on animals. Continued use of tobacco creates in man a disposition to cancer at the place of provocation. The time needed for creating this disposition varies for different persons

Members of families disposed to cancer and persons with chronic catarrils of the respiratory tracts should be dissuaded from smoking

A statistical survey was made of 96 deceased carcinoma of the lung patients, of whom 86 were males. Of these 96, 25 (2907 per cent) were extreme smokers, 18 (2093 per cent) were very heavy smokers, 13 (1512 per cent) were

heavy smokers, 27 (31 39 per cent) were moderate smokers, and 3 (3 49 per cent) were nonsmokers. Comparison of these 96 cases with 86 healthy persons as to daily consumption of tobacco disclosed that the healthy persons smoked considerably less and that most of them were moderate and medium heavy smokers. The fact that one-third of the subjects surveyed smoked moderately or not at all indicates the presence of other cancerigenic factors besides smoking, such as influenza and industrial working conditions.

Tumor

Surgical Treatment—Graded Pneumonectomy—W F. Rienhoff, Jr,8 states that the successful treatment of malignant tumors of the lung, and those of benign tumors which involve the primary bronchus rather extensively, can only be accomplished by complete removal of the lung, together with its lymphatic vessels and glands Lobectomy has been uniformly unsatisfactory

Twenty patients have had a total pneumonectomy by means of a graded pneumonectomy. The procedure, divided into several steps or grades, permits the interruption of the operation at 1 or several points when the condition of the patient does not warrant a complete one-stage procedure. However, the operation should be completed in 1 stage if the condition of the patient permits.

Of the 20 patients operated, 2 died One death was due to failure of the peripheral circulatory system and the other was due to coronary thrombosis

The proper preoperative preparation of the patient consists of the introduction of air into the pleural cavity in order to bring about a preoperative collapse of the lung. An injection into the pleural cavity of 50 cm. of beef-infusion broth, pH 745, containing 1 per cent of peptone, is also made in all cases in which

it has been possible to bring about a preoperative collapse of the lung. This injection is made from 48 to 72 hours before operation and serves a 2-fold purpose. It protects the patient against infection and acts as a stimulus to the formation of granulation tissue, the exudation of plasma, and the obliteration of dead space, which will result from the removal of the lung.

After a period of 48 hours, a lining layer of granulation tissue will be formed. In this manner a preoperative mobilization of the combative and defensive inflammatory processes of the body against local thoracic and general blood stream invasion has been accomplished.

The anesthesia for this operation consists of a combination of *nembutal* and *cyclopropane*, which has been found most satisfactory

The incision is made over the third intercostal space, anteriorly, and extends from the lateral border of the sternum to the anterior axillary line. The pectoral muscles and the intercostal muscles are incised about midway between the third and fourth ribs. The pleural cavity is then quickly opened by cutting through the parietal pleura for the entire length of the incision and the chest wall is opened by widening the incision, by means of a self-retained retractor of the ribs or a rib spreader. Resection of the ribs is not necessary.

The mediastinal pleura is incised and dissected medialward, with exposure of the pulmonary artery. The inferior surface is then dissected away from the upper border of the superior pulmonary vein, and a No 10 oiled, braided silk ligature is passed around the mediastinal portion of the vessel, at least 2 or 3 cm proximal to its intrathoracic branches. The ligature is then tied and another ligature is placed about the vessel 0.5 cm.

distally. This is likewise tied. The loose ends of these ligatures are cut at least 6 cm. long so that they and the obliterated pulmonary artery may be easily recognized if a second-stage operation is found to be necessary. The phrenic nerve is crushed.

The primary bronchus is then stripped of all the bronchial lymphatic glands and peribronchial connective tissue from the bifurcation of the trachea to the point at which the pulmonary artery crosses the bronchus and takes up a position posterior to this structure. A ligature of No. 10 braided silk is placed about the bronchus high up, just distal to the bifurcation of the trachea, and is firmly tied at once The pulmonary veins are then doubly ligated If, however, the decision has been made to grade the operation into 2 or more stages, then the ligatures may be placed loosely about the veins and left untied The ligation of the pulmonary veins may be considered the third step in the operation

Amputation of the main bronchus just distal to the primary encircling ligature constitutes the fourth step in the operation. Amputation of the hilus of the lung is performed from above downward on the left side, and from below upward on the right. No lung, peribronchial tissue, or lymph glands should be left behind.

The bronchus is cut across in the mediastinum, not far from the bifurcation of the trachea. The incision is made slightly obliquely to the long axis of the bronchus on a line running from above and lateral, to below and medial. The cut edge of the stump forms an angle of about 45 degrees with the superior border of the primary bronchus, and of about 135 degrees with its inferior medial border. In addition to the slanting direction of the incision across the bronchus, the cut is made on the bias so that

the posterior membranous portion is a trifle longer than the anterior cartilaginous wall. Interrupted fine silk sutures are then placed in the membranous portion in such a way that the curved needle picks up a portion of the posterior membranous tissue a few millimeters proximal to the cut edge. The needle is then inserted into the cut edge of the mucous membrane and the cartilaginous ring of the bronchus directly opposite. From 10 to 12 of these sutures are laid in a fan-shaped pattern. Thus, when the knots are pulled home, the relaxed and relatively tough posterior membranous wall is not only snugly fitted to the inner surface of the semicircular cartilaginous ring at all points, but also, as a result of the way in which the sutures have been placed, the membranous portion is rolled over the cartilaginous cut edge in a way corresponding to the inversion of the intestinal wall This method of closure of the cut end leaves no tension whatever upon the suture line. Two parallel rows of through-and-through mattress sutures are placed proximal to the interrupted row.

After the suturing has been completed, it is well to cover over the stump of the bronchus with some available additional tissue, usually a pedicle flap taken from the mediastinal pleura, with some underlying areolar tissue

Closure of the wound is accomplished by drawing the ribs together and inserting perichondral sutures of No 10 braided silk. No attempt is made to suture the pleura or the intercostal muscles. The pectoral fascia is drawn together with interrupted medium silk, while the skin is closed with fine silk. Within 2 weeks the wound is healed solidly, and there is no impulse or bulging during coughing.

Embolism

Etiology—E. C. Cutler⁹ states that with the advent of infiltration anesthesia, a different conception of the mechanism giving rise to postoperative pulmonary complications which formerly were thought to be due to the aspiration of, and the irritation which accompanied, inhalation anesthesia, is necessary and embolism from the field of operation is proposed.

Embolic lesions are due to what happens in the wounds of the patients. A decrease of the incidence of the embolic lesions will come only through an appreciation of the causes of thrombosis and embolism.

Roentgen Diagnosis — N. Westermark¹⁰ made roentgenologic studies in 26 cases in which embolism of the pulmonary artery was subsequently established at necropsy. In all these cases the roentgen examination was carried out within 2 weeks of the patients' death. In 12 of them, a roentgenogram was made during the last 2 days before death. In the majority of the cases, the examinations were repeated so that it was possible to follow the development of the embolus

Ten of the 26 cases presented signs of pulmonary infarct, while the others were free from infarction. The roent-genologic diagnosis of embolism of the pulmonary artery is difficult, particularly in cases without infarction. However, careful analysis of the roentgenograms taken in different directions and preferably on repeated occasions makes it generally possible to arrive at a correct diagnosis.

Emboli with and without infarction each present their own typical roentgenologic aspects. In embolism of the pulmonary artery without infarction, there is ischemia of the branches of the pulmonary artery on the peripheral side of the embolus. On the roentgenogram this ischemia appears as a clarified area with diminished vascular design corresponding to the extent of the embolized artery. The vascularization is maintained in the central parts of the lung. The infarct appears on suitable projection as a wedge-shaped massive homogeneous shadow. However, in most cases in which infarction is present, it is possible to observe also within other parts of the lung larger or smaller wedge-shaped clarifications as in embolism without infarction.

Treatment—E. C. Cutler⁹ states that after the occurrence of embolic lesions, therapy should be aimed at restoration of an adequate circulation, adequate care of wound infection, and treatment of oral sepsis with arsenical drugs.

Pneumonoconiosis

Etiology—Silicosis and Its Relation to Tuberculosis—T. O'Leary¹¹ states that the co-existence of silicosis and tuberculosis, in the same lung, seems to evidence a mutual enhancement of the one disease by the other

Besides the well-known industries in which silica occurs, such as mining and quarrying, silica is used in the manufacture of many common articles like. soaps and scouring powders, tooth powders and pastes, paint, fertilizer, sand paper, optical lenses and insulation for pipes.

A case of silicosis has been reported in a tap dancer who sprinkled sand on the floor to keep himself from slipping

Diagnosis—T. O'Leary¹¹ reports that the diagnosis of silicosis depends on a history of adequate exposure to silica dust. There must have been at least 2 years of work in a heavy concentration of fine silica dust.

From the x-ray standpoint, simple discrete nodulation and massive conglomerate fibrosis with or without generalized nodulation, constitute the manifestations of silicosis.

Symptoms vary with the type of lesion. Simple discrete nodulation has little clinical expression, but exercise tests may show slight changes in the pulse and respiratory rate. With conglomerate fibrosis, however, dyspnea is a marked symptom. When active tuberculosis is present, symptoms of intoxication may be masked and bacılli may not be found in the sputum until just before death.

Treatment—T O'Leary¹¹ states that the treatment of silicosis is primarily prophylactic. There is no drug or other form of therapy known which will dissolve fibrous tissue in the lungs and restore a damaged lymphatic system.

Silicosis is a preventable disease by means of adequate ventilating and dust exhaust systems.

The elimination of sources of tuberculosis infection in industries where silica dust is a hazard is of equal importance. This can only be accomplished by systematic examination, early diagnosis and repeated x-ray studies of individuals engaged in occupations involving exposure to silica dust.

MEDIASTINUM

Periesophageal Abscesses

Diagnosis—W M Hunt¹² states that cervical periesophageal infection follows a rupture of the esophagus caused by foreign bodies, instrumentation, or spontaneous rupture accompanying malignancy.

A diagnosis of infection of the mediastinum is suggested by the suspected or observed perforation by a foreign body, instrument or malignancy; by the

marked collapse of the patient observed at the time of perforation; pain, tenderness and swelling over the area; the inability to swallow; the absence of dyspnea unless a pneumothorax has occurred; an increase in the leukocyte count of from 15,000 to 23,000 (usually the higher); a sudden temperature rise (although seldom higher than 103° F -395° C.), definite x-ray evidence of a widening of the prevertebral or posttracheal space, and emphysema which may be readily ascertained by palpation or observation or which may be recognized only by roentgenological exam-The roentgenogram is the determining factor in diagnosis and is of aid in the differentiation between a simple cellulitis, which might disappear, and an abscess formation with a bubble of air Daily roentgenograms should be made following any known perforation

Prognosis — W M. Hunt¹² states that untreated cases are fatal if a real abscess has developed. The mortality is low if dramage is thoroughly established while the infection is localized in the region of the perforation.

Treatment—Immediate external incision and drainage should be instituted. Intra-esophageal treatment should be used only in the most selected cases. It is better surgery deliberately to open and pack off any known esophageal rupture before an abscess has developed harly drainage of these areas is definitely indicated.

Anterior Longitudinal Mediastinotomy—1' Lyraga¹³ reports that by means of an anterior longitudinal thoracotomy with section of the sternum, a method originally devised by Milton and now commonly accepted, a sufficiently wide operative field is obtained and the various endothoracic viscera may be conveniently exposed, for such conditions as diseases of the great vessels, inflammatory or neoplastic processes of the anterior mediastinum, traumatic lesions of the heart and the lungs, and wounds or tumors of the lung.

A median incision is made which extends from the inferior margin of the thyroid cartilage to the ensiform process. The sternum is bisected with a saw and with the aid of a bone chisel The sectioned parts of the sternum are retracted and the posterior and interclavicular ligaments are severed. The delicate pleural reflection is peeled off with the aid of the fingers, special care being taken to avoid tears. In repairing the wound, the sectioned sternal margins are approximated and are sutured with metallic stitches which are introduced with the aid of a perforator. The overlying fascia and skin are repaired in the usual manner

Of 2 patients operated upon in this fashion, the first presented a lymphosar-coma occupying the anterosuperior mediastinum and the second had a large retrosternal sarcoma. Following an anterior longitudinal mediastinotomy, a biopsy specimen of the tumors could be obtained. Following irradiation, both patients made an uneventful recovery

German surgeons describe 3 varieties of anterior longitudinal mediastinotomy total anterior longitudinal mediastinotomy (Schoene), longitudinal anterosuperior mediastinotomy, and longitudinal anteroinferior mediastinotomy (Sauerbruch)

Anterosuperior longitudinal mediastinotomy gives the most satisfactory results. In this operation, the sternal heads of the sternocleidomastoid muscles are resected under local anesthesia, the superficial veins are ligated, and with the aid of the fingers, the posterior surface of the sternum is carefully freed from the underlying pleura and the great vessels. The internal mammary vessels are either pushed laterally or they are ligated. Subsequently, the sternum is sectioned by means of a sternotome. The operation is indicated especially in aortic aneurism, in neoplasms of the mediastinum and in various carcinomatous processes involving the lungs and their hila.

PNEUMONIA

Pneumococcic Pneumonia

Treatment—H. F. Flippin¹⁴ states that American and British reports are encouraging in the treatment of pneumococci pneumonia with *sulfapyridine* (M & B 693)

Initiation of the drug treatment is followed within 24 to 36 hours or less by a critical drop in temperature This temperature drop is not immediately accompanied by any significant change in the lung signs, but always reflects a marked improvement in the toxemia and general well-being of the patient Resolution of the pneumonia then follows within a variable period of days cannot be said whether resolution is hastened or retarded by the fall in temperature The critical drop in temperature is followed within 12 to 24 hours by a marked drop in the total leukocyte count. This is believed to be a favorable sign, since in cases where the white blood count remains elevated, despite adequate drug therapy, the usual clinical improvement is retarded. In some instances there is a recurrence of low grade fever which persists for several days after the initial drop

At this time there are no definite rules as to the amount of drug that should be given, due to inability to predict what constitutes an effective blood level of sulfapyridine in patients with pneumonia. Thus far, experience fails to show any correlation between the blood

sulfapyridine level and the therapeutic effect. The blood levels were found to be uniformly high in elderly individuals and in young persons with renal impairment.

On the basis of past experience, the following dose schedule is used in adult patients:

An initial dose, by mouth, of 30 grains (2 Gm), followed every 4 hours by 15 grains (1 Gm.), until the required total dosage as outlined below is given:

- 1. Patients treated during the first 5 days of the disease receive a total of 375 grains (25 Gm)
- 2. After the fifth day 225 grains (15 Gm.) is sufficient in most cases
- 3 All cases of bacteremia should receive at least 375 grains (25 Gm) and usually more; sometimes a total of 750 grains (50 Gm) is necessary.
- 4 In elderly patients and those with renal involvement, a total dosage of 225 grains (15 Gm) will often suffice
- 5 When there is evidence of spread in the pneumonia, despite a normal temperature, a larger total dose is advisable
- 6 In cases where specific serum has been used without apparent success, sulfapyridine should be given as outlined above
- 7 The failure of a patient to show clinical improvement after 48 hours of adequate sulfapyridine therapy, is considered by some as an indication for specific serum

In the treatment of infants and children, the total dosage has varied with the individual case. One and one-half grains per pound of body weight every 24 hours in divided doses has been given

B R Allison¹⁵ treated 100 cases of pneumonia at the Nassau Hospital since January, 1939. Every pneumonia patient was given sulfapyridine whether or not a pneumococcus was found in the sputum

An initial dose of 30 grains (2 Gm) of the drug followed by 15 grains (1 Gm.) every 4 hours was given in most of the adult cases. Of the 58 adults, 28 received a total of less than 4 drams (15 Gm.), 15 received from 4 to 6 drams (15 to

25 Gm.), 10 from 6 to 10 drams (25 to 40 Gm.), and 5 more than 10 drams (40 Gm.). The average total dosage was 4¾ drams (19 Gm.). Small doses, certainly much smaller than the 6 drams (25 Gm.) originally suggested, prove sufficient in many cases.

In children, a daily dose of 1½ grains per lb. (0.2 Gm. per kg.) of body weight, reduced to ⅔ grain per lb. (0.09 Gm. per kg.) after the first 24 hours is suggested. Children seem to tolerate the drug so well that in some cases much larger amounts have been given. The average total dosage for children was 1¾ drams (7 Gm.). This total dosage was well tolerated by each of the 9 infants.

Sixty-one patients were admitted before the fourth day of the disease, 20 on the fourth day, and 19 after the fourth day. Forty-two cases were children less than 10 years of age and 9 of these were in their first year.

The sputum was examined at least once, in 97 cases Twenty-seven were negative for pneumococci Twenty-two of the 27 patients in whose sputums no pneumococci were found, showed a prompt response to treatment. It is possible that further sputum examinations would have revealed pneumococci; otherwise such a high percentage of prompt responses in nonpneumococcic pneumomas would not be expected

Pneumococci, types I, III to VIII, XI, XIV to XXIII, XXVIII, and XXIX, were found in the other 70 cases Blood counts and urmalyses were done in all cases. If a patient was desperately sick on admission or did not respond promptly to the drug, serum also was given. The severity of illness of these 100 cases was comparable to any similar series of patients with pneumonia admitted to the hospital in recent years. The average number of days spent in the

hospital was 13.8. Four of the patients died, 1 infant and 3 adults.

The mortality rate at the Nassau Hospital for all pneumonias during the last 4 years was 19 per cent in 1935, 20.9 per cent in 1936, 18.1 per cent in 1937, and 11 per cent in 1938.

Six of the 70 blood cultures done were positive in the 1939 series. Three were type I, 2 were type VIII, and 1 was unidentified. One of the patients with type I pneumococci, with a very heavy growth, was addicted to alcohol, had hypertension, and made a dramatic recovery. One, with a heavy growth, died in 24 hours in spite of 400,000 units of serum and sulfapyridine. The third patient recovered after 300,000 units of serum and 46 Gm of the drug Both patients with type III pneumococci recovered The unidentified case also resulted in recovery.

Usually, the temperature showed a marked drop in from 12 to 36 hours after administration of sulfapyridine and with this, the pulse and respiratory rate dropped. The general appearance and sense of well-being of the patient showed a corresponding improvement. The temperature response seems to be a good index of the extent of improvement. There were no serious toxic signs in any of the cases.

In order to avoid the extra work generally involved in determining the sensitivity of the different pneumococci to sulfapyridine, I. H. Maclean, K. B. Rogers and A. Fleming¹⁶ adopted a method in which a fixed amount of sulfapyridine was added to blood infected with various dilutions of a pneumococcus culture. This permitted obtaining an end point with an unknown culture without any preliminary titration. Using a strength of 1 in 20,000, 30 types of pneumococci were tested.

The pneumococci vary enormously in their sensitivity to sulfapyridine and the variation is not associated with the type of pneumococcus but with the individual strain. Animal experimentation confirms the results obtained *in vitro*, suggesting that whenever possible, such a test should be carried out and according to the result obtained, forecasts can be made as to the result likely to be obtained with sulfapyridine treatment.

If the infecting organism is sensitive, simple treatment with the drug will probably be effective. If it is only moderately sensitive, it is likely that some increase in immunity will be necessary in addition to sulfapyridine treatment. However, if the organism is insensitive to sulfapyridine in concentrations which can be attained in the human body, there appears to be no justification for embarking on a course of treatment, which apparently cannot do good and may have serious toxic effects.

Animal experimentation indicates that the combined use of vaccines and sulfapyridine in man is beneficial in all cases of pneumonia.

Animal experimentation shows that pneumococci can, in an infected animal treated with sulfapyridine, readily establish a tolerance or fastness to the drug This makes it essential that the initial doses should be large. Also, as sulfapyridine merely interferes with the growth of the bacteria and the body has to do the actual killing, it is essential that the immunity be raised to as high a degree as possible by any means, active or passive, specific or nonspecific, so that the destruction of the bacteria may be complete before tolerance of the pneumococci to the drug has been established

Toxic Effects of Sulfapyridine—As with sulfanilamide, the toxic effects of sulfapyridine are sufficient to require close observation of the patient and careful usage of the drug. The most

troublesome and most frequent untoward effects of the drug are nausea and vomiting. Both are most likely to appear during the first 24 hours of treatment and are probably of central origin, rather than local gastric irritation. The following methods have been used to control the nausea and vomiting and in individual cases, each of these adjuvants appear to improve the tolerance for the drug:

- 1. The administration of small amounts of sodium bicarbonate after ingestion of the drug.
- 2. Mixing of the drug with water, fruit juices, or milk.
- 3. Omission of treatment for 1 or 2 doses, followed by its resumption.
- 4. The use of barbiturates and chloral hydrate.
- 5. The introduction of **sodium chloride** and **dextrose**, intravenously, is advisable in all patients who show nausea and vomiting. This appears to be a valuable method of minimizing these symptoms as well as of restoring normal fluid and electrolyte balance in the patient who is vomiting.

The extreme insolubility of the drug has made impractical its administration through the rectum. The use of an enteric coated tablet by mouth has been unsuccessful

Other toxic reactions include cases of transient hematuria, dermatitis, acute hemolytic anemia, leukopenia, drug fever, and agranulocytosis reported by F. D Johnston.¹⁷ Cyanosis does occur, but its presence does not necessitate the withdrawal of the drug. Aside from the nausea and vomiting, these toxic reactions do not occur as frequently with sulfapyridine as with sulfanilamide

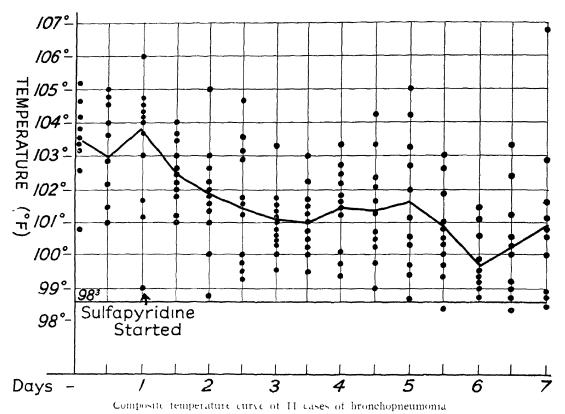
In view of the above toxic effects, it is advisable to watch the urine closely for red cells, acetone and urobilin, and the blood count for signs of progressive anemia and neutropenia. In elderly patients the blood urea nitrogen level should be checked and, in those with severe

vonuting, blood chloride studies are indicated

Sulfapyridine in Treatment of Pneumonia in Children—H Lowenburg, Jr, 1st used 1 grain per pound (0132 Gm. per kg.) per day This was divided into 6 4-hour doses over a period of 24 hours. In most instances, the sulfapyridine was given for 3 days.

to normal Concomitant with the fall in temperature, there was noted an immediate improvement in the general condition of the patient. Three children, who were moribund, were sitting in bed playing the following day

The pathology was not materially affected. Both clinically and by roentgenogram, the pneumonic process progressed



The initial dose was $1\frac{1}{2}$ to twice the amount of the other 4 hourly doses. An alkali (sodium citrate) was given in conjunction with the sulfapyridine in suitable doses. Other treatment consisted of general supportive measures.

Of 23 children treated with sulfapyridine, 12 had lobar consolidations and 11 gave evidence of patchy involvement

All 12 patients with lobar consolidations gave immediate responses to the institution of sulfapyridine therapy. In only 1 patient did it require more than 30 hours for the temperature to drop in its usual manner. As all these patients were treated early, the critical fall in the temperature may reasonably be attributed to the sulfapyridine.

The following chart gives a composite picture of the temperature curves in the 11 patients with bronchopneumonia

The course of the disease was not materially affected by sulfapyridine, whether or not the drug was used early or later. In this group of 11 patients, there was a mortality rate of 18 per cent. These findings differ from those of G. M. Evans and W. F. Gaisford¹⁹ and those

of H. L. Barnett, A F Hartmann, A. M. Perley, and M. B Ruhoff²⁰

Treatment of Postoperative and Primary Pneumonias—H. C Hinshaw and H J Moersch²¹ treated 21 cases of postoperative pneumonia and 6 cases of primary pneumonia with sulfapyridine. Usually 15 grains (1 Gm) of sulfapyridine was given by mouth every 4 hours day and night.

The diagnosis of pneumonia was confirmed by roentgen examination in every case Sulfapyridine usually was withheld until there was evidence of serious progressive pneumonia. Most patients received nonspecific supportive treatment Three patients received positive pressure therapy for pulmonary edema, with successful results At least half of the patients were so seriously ill that recovery would have been doubtful without sulfapyridine or specific therapy. More than half of the patients with postoperative pneumonia were 55 years of age or more. Only 4 patients were less than 45 years of age

The drug was equally effective in the treatment of both elderly and young patients. The maximal temperature of nearly half of the patients approached normal within 24 hours after treatment with sulfapyridine was begun. The condition of most of the others was significantly improved in from 48 to 72 hours.

Postoperative, as well as primary pneumonia, responded. Only 1 death occurred. This was in a case of early fulminating postoperative pneumonia which developed on the second day after extraperitoneal resection of a carcinoma of the colon. Some patients, who did not respond to other treatment, did subsequently respond to sulfapyridine.

Treatment of Pneumococcic Pneumonia Complicating Pulmonary Tuberculosis—J H Crawford²² obtained no improvement from routine treatment

of a case of pneumococcic pneumonia superimposed on a pulmonary tuberculous lesson until *sulfapyridine* was administered to the patient on the sixth day of illness

The mitial dosage (15 grains—1 Gm. every 4 hours) was not high and as no toxic effects were observed, higher doses probably could have been given with safety. The drug was discontinued after 5 days which apparently was a little premature in this case as slight relapse followed. This was easily controlled by further administration of sulfapyridine in the same dosage as before

There was no increase in activity of the tuberculosis as a result of the infection, and subsequent x-ray examination of the chest revealed a definite improvement in the nature and extent of the tuberculous lesion

Lobar Pneumonia

Treatment—M. Cutts, C. F. Gormly and A. M. Burgess²³ state that of 84 patients with lobar pneumonia treated at the Rhode Island Hospital, only 22 were treated only with *serum*, 44 were treated with *sulfapyridine* alone, 13 with serum and the drug, and 5 who entered the hospital after the fifth day of their disease received no drug or serum therapy.

Patients given both the drug and serum were not chosen because of any greater severity of their illness. Severe pneumonia was present in all groups in about equal proportions. The duration of the disease at the time of admission averaged 24 days in the serum treated group, while those in the drug therapy only group averaged 32 days. In those patients who received combined treatment, the average duration was 2 days.

The average age of the drug treated patients was 42 years, the average age of the serum treated cases was 42, and the

average age was 50 years in those who received both serum and drug therapy.

In the great majority of cases, sulfapyridine exerts no serious toxic effects if used in proper dosage. However, nausea and vomiting are quite troublesome. Occurrence of both rash and drug fever was noted in 2 patients receiving more than 10 drams (40 Gm.) of the drug, suggesting that such large doses should be used with caution. Agranulocytosis or acute hemolytic anemia was not encountered in the cases treated but their known occurrence in occasional cases makes frequent blood counts and close observation essential.

There was 1 death among the patients receiving sulfapyridine alone, 3 deaths among those treated with serum and the drug, 2 deaths in the serum treated patients, and 3 deaths among the 5 patients admitted to the hospital after the fifth day of illness who received no treatment.

Taking into consideration the number of lobes involved, the duration of the disease when treated, blood cultures, age of patient, type of infecting organism, temperature response and presence of complications, 90 per cent of the drug treated cases yielded good results as compared to 73 per cent of the serum treated group

Sulfapyridine was equally effective in all types of pneumonia, with the exception of that caused by the type III pneumococcus.

THORACIC SURGERY

Rib Regeneration — According to W. F. Bowers²⁴ there are 3 main schools of thought on the theories of osteogenesis and bone repair.

1. Periosteal regeneration. Many regard the periosteum and endosteum as definite organs for the formation and repair of bone. Accord-

ing to this theory, osteoblasts never arise from adult bone cells, but from the cells of the periosteum and, to a lesser extent, from the endosteum.

- 2. Osteoblastic regeneration. The proponents of this theory uphold 1 of the 2 following opinions: (a) After injury bone cells are liberated from their lacunas and these multiply to form new bone; (b) after injury wandering connective-tissue cells are drawn to the site of reaction and through their pluripotentiality become osteoblasts.
- 3 Extracellular deposition of calcium salts. This hypothesis holds that there is no definite bone-producing cell but that after injury calcium salts are laid down in the framework of the adjacent connective tissue by chemotaxis. These connective-tissue cells then become bone cells by metaplasia or by functional adaptation

Regarding the problems of bone transplantation, regeneration of bone, heterotopic osseous formation and chemical inhibition of rib regeneration:

- a The periosteum is definitely osteogenic and is a very important source of blood supply to bone.
- b The periosteum is the most important source of regeneration of bone and its presence is necessary for union in case of fracture.
- c. The growth of osseous and periosteal transplants is in direct ratio to their ability to establish an adequate blood supply
- d. A solution of formaldehyde is superior to Zenker's solution as an inhibitor of costal regeneration, the inhibition which it produces lasting for at least 4 months. The application of a solution of formaldehyde USP, diluted 1 to 10, to the periosteal beds, apparently is not accompanied by delayed healing of the wound or by any other disadvantage. It is advocated in all resections of the ribs for the drainage of empyema or abscess of the lung. It is also advocated in first-stage thoracoplastics, except that it should not be used in the bed of the first rib because of possible damage to the adjacent nerves and vessels by the formation of scar tissue.

The chemical inhibition of rib regeneration should not be employed in the Semb type of apicolysis, because in this operation the new bone aids in maintaining collapse of the lung.

TUBERCULOSIS

Etiology—H. I. Spector,²⁵ reporting on marital tuberculosis (the development of clinical tuberculosis in both husband and wife), states that judging from 208 responses received in answer to 304 questionnaires sent to a selected group of phthisiologists in the United States and in certain European and South American countries, the majority of physicians approve of marriage between tuberculous individuals and between tuberculous and nontuberculous individuals. In Germany, however, marriage between tuberculous and nontuberculous persons is forbidden by law.

The majority of the phthisiologists approved of their arrested tuberculous patients having children although the answers received from the doctors in France stressed the importance of vaccinating the newborn child with BCG vaccine at the time of birth.

A study was made of 11,193 cases of tuberculosis reported in St. Louis for the 10-year period from 1928 to 1937, inclusive. Among these patients there were 5514 married persons and, among these, there were 210 couples with marital tuberculosis. This is an incidence rate of 3.8 per cent marital tuberculosis per 100,000 married tuberculous as compared with a tuberculosis incidence rate of 0.13 per cent in the general population In other words, the risk of infection and development of clinical disease in a healthy man or woman in marital contact with a tuberculous mate is 29 times greater than in the general population.

Marital tuberculosis is not as infrequent as is generally believed and the evidence indirectly suggests that exogenous reinfection may be responsible for tuberculosis in the consorts.

Analysis of the statistics of the 210 couples with marital tuberculosis also

showed that 55 (9 per cent) of their 595 contacts contracted tuberculosis. Thus the incidence of tuberculosis in contacts of marital tuberculosis is 9 per cent as compared with the incidence of 0.13 per cent in the general population. In other words, a child exposed to 2 tuberculous parents has 69 times more chance to develop tuberculosis than if he were exposed to the general population.

Complications—Pregnancy—F. M. F. Meixner²⁶ states that in some cases of tuberculosis, particularly advanced active cases, abortion acts as a stimulus to the chest lesion, and noninterference is preferable if it is felt after careful observation that abortion will mean death for both mother and child, while allowing progress of the pregnancy may mean death of the mother, thus sacrificing everything for a live child

Early induction of labor and forceps delivery may be indicated. With collapse therapy, even these apparently hopeless cases can often be carried through a normal pregnancy and delivery, treatment being continued after delivery. By doing a phrenectomy or phrenic crush and using greater than usual pressure by pneumothorax, and, in selected cases, holding the diaphragm by use of pneumoperitoneum after delivery, the prognosis is materially improved The efficacy of collapse therapy may limit the indications for therapeutic abortion in this type of case

In most cases of tuberculosis, however, it is best to remove the pregnancy and let the woman have all her facilities for conquering the tuberculosis. Then, after the danger from tuberculosis is past, she may produce the offspring she desires.

In a large group which is rapidly becoming larger as a result of early diagnosis and collapse therapy, selected by careful observation, with the patient constantly under good sanatorium treatment,

the fetus may be preserved and therapeutic abortion may be withheld. Artificial pneumothorax often brings an active lesion under control and pregnancy may proceed without complication. Moreover, if the lesion is well collapsed, it is usually not necessary to separate the mother and infant after delivery to prevent infection by tuberculosis of the infant from the mother.

With a better and more intelligent understanding of the question of pregnancy and tuberculosis on the part of the tuberculosis specialist and the obstetrician, the pregnant tuberculous patient may emerge from her pregnancy experience (once looked upon as a most dangerous and unjustifiable happening) almost, if not quite as safely as the nontuberculous woman and the lives of a large number of infants may be saved

Lactation should not be permitted as it increases the hazard for the mother by using her recuperative and healing powers for the production of milk. Also, in open cases, there is great danger of the infant acquiring a tuberculous infection from the mother.

In the decision to interfere by abortion, the social aspect must also be considered because in many instances a woman would be unable to take care of her child and her home surroundings would not be proper for the welfare of the baby, which makes it necessary to terminate. The problem here, like the entire problem of tuberculosis, is not only medical but social. The religious aspect of the problem is purposely omitted from discussion but must be borne in mind when outlining treatment for any given case.

The principles to be followed are:

First, no one has shown definitely that pregnancy is good for the health of a tuberculous woman in any stage or type of tuberculosis. A neutral effect of

pregnancy on a tuberculous lesion is not asked as the risks are too great.

Second, about 75 per cent of investigators believe that pregnancy aggravates tuberculosis, while no one has proved that abortion, properly performed, aggravates an early, quiescent or arrested lesion, if proper tuberculous therapy is followed afterward

Third, pregnancy places a severe strain on a tuberculous woman's resources and strength and labor is fraught with immediate and remote perils.

Fourth, the fate of the patient does not depend on the fact that she is pregnant, but rather upon the character of the chest lesion and upon the care she receives during pregnancy and puerperium

Fifth, after labor or abortion, treatment of the chest condition should be carried on vigorously, and must be continued over sufficient time to guarantee arrest and should not be discontinued too early, and only after very careful observation and study by an experienced phthisiotherapist

Subsequent pregnancies should be allowed only after careful study of the case has shown the chest lesion completely arrested or under complete control

Sixth, therapeutic abortion should be done as early as possible when decided upon, but after the fourth month of gestation the effect of intervention is comparable to a full term delivery. With proper collateral care in cases that have not shown an acute flare-up earlier, the risk can be safely assumed, the physician being ready to interfere as soon as labor starts so as to terminate rapidly, as by forceps, sparing the patient the stress of inhalation anesthetics.

Extrapulmonary Tuberculous Complications—D Perla and S B. Biller²⁷ analyzed 1116 postmortem examinations of patients dying from pulmonary tuberculosis.

Larnygeal involvement occurred in about one-third of the cases. Tuberculous enteritis complicated pulmonary tuberculosis in more than half of the cases. In cases of tuberculosis of the larynx, tuberculosis of the intestine generally develops. The epididymis was practically never involved without the presence of a tuberculous focus in the prostate. Tuberculosis of the genital tract is a ready source for further hematogenous dissemination. Gross renal tuberculosis was absent in more than 90 per cent of the 1116 cases.

In general, involvement of the larynx and intestine occurs in active progressive diseases of the lungs but renal and genital tuberculosis are associated with fibrotic pulmonary lesions or hematogenous pulmonary tuberculosis. Amyloid disease is particularly prone to develop in tuberculous patients with extensive extrapulmonary complications.

Bronchopleural Fistulas and Tuberculosis—O Auerbach and S Lipstein²⁸ state that in 1000 consecutive necropsies in chronic ulcerative pulmonary tuberculosis, 78 cases of bronchopleural fistulas were found

Fifteen of the bronchopleural fistulas occurred in previously uncollapsed lungs 56 in the presence of an artificial pneumothorax, and 7 as a direct result of closed pneumonolyses. The fistulas were diagnosed clinically in 52 cases. The size of the fistulas at necropsy varied from 1 mm to 4 cm and 73 per cent were present in the upper lobes of the lung.

Bronchopleural fistulas occurring within 6 months after the induction of artificial pneumothorax usually ended in a fulninating caseous pneumonia. The underlying pulmonary pathologic condition in cases of bronchopleural fistulas occurring after from 1 to 4 years of pneumothorax therapy was that of a chronic pulmonary tuberculosis Empy-

emas were present in all but 5 instances. In these, the fistulas developed too soon before death for fluid to collect. Mixed infection empyemas were recorded in 27 instances, tuberculous empyemas occurred in 17 and the remaining patients either had no aspirations or the reports were inadequate.

Healing of bronchopleural fistulas may be temporary or permanent. It may occur because the visceral pleura becomes adherent to the parietal pleura in the region of the perforation or a fibrinous exudate, which later is organized into fibrous tissue may seal off the opening.

Cervical Lymphadenitis—B. C. Thompson²⁹ states that scrofula, which has been called "the king's evil" and "the necklace of boils," was called gāndamāta by the ancient Hindoos in the year 500 B C. Scrofula, which is tuberculosis of the lymphatic glands, and sometimes of the bones and joint surfaces, is essentially a disease of early life. It is a disease of ancient lineage and worldwide distribution and was recognized from the earliest times although its relationship to tuberculosis was not definitely established until the era of Koch

Formerly, its occurrence was almost universal, sometimes epidemic in form, among all civilized communities. Today, however, its occurrence has been reduced to a greater degree than pulmonary tuberculosis and it has almost vanished from the communities of United States and Canada This is probably due to the eradication of tuberculous cattle and the almost universal pasteurization of milk In British India, however, it is a common condition today Here the milk is generally boiled before use. It is also common in China and Japan, where milk is not used to any extent, and the age distribution is very similar to that of pulmonary tuberculosis.

A study made of 324 cases registered at a tuberculosis dispensary in Great Britain during the years 1934 and 1936, when there was extensive unemployment and excessive overcrowding and malnutrition, and the average milk consumption was % of a pint (200 cc.) per person per week, disclosed 20 per cent of the cases were classed as suffering from tuberculosis of peripheral lymph nodes. The majority of the cases occurred between the ages of 5 and 15 years.

Sometimes there were positive indications that the initial lymphadenitis was a primary infection phenomenon, such as when it was accompanied by an outbreak of erythema nodosum or of phlyctenular conjunctivitis, signifying an abrupt rise in allergy. The age distribution corresponded fairly closely with that of primary tuberculous infection, as far as information was available from routine tuberculin testing.

Contact with positive sputum tuberculosis was established in 21 per cent of the cases, as compared with a positive sputum contact of 36 6 per cent in a similar series of patients with pulmonary tuberculosis. This suggests the possibility of a bovine tuberculosis etiology in many cases. However, the disease was uncommon before the age of 5 years and it has been reported that the highest incidence of bovine infection is found in the first 5 years of life. In districts where bovine tuberculosis is common, the majority of cases of cervical lymphadenitis occur in the 0 to 5 years age group

Among these cases studied, the exceedingly low consumption of milk and butter among the population does not suggest a bovine etiology.

The period of maximum incidence was when the incidence of pulmonary tuberculosis and the death rate from all forms of tuberculosis was very low. Though theoretically cervical lymphadenitis may arise secondarily to abdominal tuberculosis, there was no evidence in the series of cases that this took place more than exceptionally.

Only exceptionally was there any indication of a hematogenous infection of lymph nodes. In rare instances of generalized lymphadenitis, the disease appeared in successive lymph node groups over a period of years, never simultaneously. Almost always, the first manifestation was in a lymph node adjacent to a nasopharyngeal, pulmonary, or (as in the 11 cases of inguinal lymphadenitis) alimentary portal of entry, from which the disease spread regularly along lymphatic route Lymph nodes remote from these portals, such as the epitrochlear or popliteal groups, were seldom affected and other evidence of blood borne spread, such as tuberculosis of the skin or bone or joints, was uncommon except as sequel to long established tuberculous lymphadenitis

The 324 cases of cervical lymph nodes observed, fell into 2 classes, those of nasopharyngeal origin, beginning in the upper cervical groups and spreading downwards, and those of pulmonary origin, beginning in the lower cervical groups, and spreading upwards. The former outnumbered the latter 5 to 1.

When the total cases of involvement of each lymph node group are distributed according to age, it is found that the upper cervical groups approximately coincide, and when combined together, they describe a curve very different from that of the combined lower cervical groups. In the former, most of the cases fall between the ages of 2 and 15 years, rising abruptly to a peak at 8½ years, while the latter show a much broader distribution gradually reaching a maximum at the age of 13 years. This later and less regular appearance of supra-

clavicular and axillary lymphadenitis is dependent upon its respective original source. Spread from the upper cervical groups, a process which sometimes occupies several years, or extension from pulmonary tuberculosis, is a condition commoner after puberty.

The upper deep cervical group of lymph nodes was involved almost as frequently as all the other groups combined. This involvement was often bilateral and in two-thirds of the total cases, the disease started in this group before spreading to others. The mesial subgroup is commonly termed the tonsillar group because it drains directly the faucial tonsil. The pharyngeal tonsil (adenoid) is drained by the lateral or external subgroup. In a large number of cases of tuberculosis of the upper deep cervical lymph nodes, microscopical tubercles have been demonstrated in tonsils and adenoids which appeared normal to the naked eye. Probably, tuberculosis, in a previously uninfected subject, gains entrance by the nasopharvnx in a manner analogous to that in which it gains entrance by the lung, with the formation of a primary complex, of which the inoculation site in the tonsil remains clinically latent while tubercle bacilli multiply and produce massive caseation in the regional lymph nodes

Patients in whom the preauricular, submaxillary, or submental groups of lymph nodes became involved, showed involvement also of the homolateral tonsillar group of lymph nodes in a large number of cases. Since the normal path of lymphatic drainage of these groups is towards the tonsillar group, this might be expected but it is significant that in more than half of these cases the disease appeared in the tonsillar lymph nodes earlier than in the other groups Retrograde spread of this type, contrary to the normal lymph flow, was seen re-

peatedly in other parts of the body and seems an important feature of lymphatogenous tuberculosis. Probably, in the majority of cases, lymphadenitis in the preauricular, submaxillary and submental groups was secondary to tuberculosis of the corresponding upper deep cervical nodes, presumably infected through the tonsils.

Tuberculosis of the upper deep cervical, preauricular, submaxillary and submental lymph nodes, which may be classed together under the term "upper cervical group" tended to spread downwards by 1 of 2 paths: by the internal jugular chain in the line of the carotid artery or by the external jugular chain which runs obliquely across the posterior cervical triangle. In either case, lymph nodes in the path of drainage became involved and infection might reach the supraclavicular lymph nodes from which it sometimes spreads to the axillary group.

The supraclavicular and axillary groups, which are anatomically in close relation, were frequently involved together in the same patient.

In 42 of the cases, one or the other of these 2 groups was the seat of the initial lymphadenitis which then spread upwards in a retrograde direction, sometimes as far as the upper deep cervical lymph nodes, by way of either the internal or external jugular chain.

In the cases of initial involvement of the supraclavicular or axillary lymph nodes (the lower cervical groups), those patients who were x-rayed showed evidence of intrathoracic tuberculosis in every case, as compared with one-third of the patients initially attacked in the upper cervical groups. This suggests that the infection, in these cases, was derived from the lung. Since there is no direct lymphatic connection between the lymph nodes of the thorax and those of the

neck, it is supposed that disease in the lung parenchyma extended from the visceral to the parietal pleura and then by afferent lymphatics to the supraclavicular or axillary lymph nodes.

There is a particular lymph node of the internal jugular chain in the "mid-jugular group" which on 7 occasions became the seat of acute isolated enlargement and caseation in each case, preceded by progressive tuberculosis in the lung apex of the same side. This lymph node has been shown, in the cadaver, to drain the dome of the parietal pleura by an afferent lymphatic, distinct from those which pass to the supraclavicular lymph nodes.

Female patients outnumbered the males in the proportion of 1 to 28. This preponderance is greatest in the years of puberty through adolescence, a period of excessive incidence, among girls, of pulmonary tuberculosis, with a raised mortality in consequence.

The apparent benignity of tuberculous cervical lymphadenitis in regard to life is illustrated by the fact that only I case died as a direct result of scrofula. This patient, aged 12 months, developed meningitis I year from onset. In addition, of 54 patients who developed pulmonary tuberculosis, 13 died.

Pulmonary tuberculosis is a complication which ordinarily affects the good prognosis of scrofula. One may read in the ancient Susruta text, dated about 500 B.C., that the ordinarily favorable prognosis of scrofula becomes hopeless if the patient develops cough, chest pain, fever or vomiting

The occurrence of pulmonary tuberculosis is probably not greatly affected by whatever treatment is adopted for the primary condition. However, by means of routine x-ray examinations, it is possible to detect pulmonary infiltration at an early stage, often prior to the appearance of symptoms, and while it is amenable to treatment. Routine x-ray examinations should be done on all cases of tuberculous cervical lymphadenitis and the observation should be continued through adolescence and young adult life.

There is no evidence that pulmonary tuberculosis which coexists with or succeeds tuberculous cervical lymphadenitis is any more benign than pulmonary tuberculosis in general.

Cases of lymphadenitis beginning in the supraclavicular and/or axillary group may already have pulmonary tuberculosis

The prognosis should be guarded whenever the existence of pulmonary tuberculosis is suspected.

Tuberculous Tracheobronchitis— J S. Packard and F W Davison³⁰ state that it is now definitely established that tuberculous involvement, particularly of the larger air passages, is a fairly common occurrence in the presence of tuberculous pulmonary disease

The mode of infection is still debatable but it appears that the most frequent avenue by which the bronchial mucosa becomes infected is along the bronchial mucous glands which extend from the bronchial mucosa to the peribronchial alveoli, lymphatics and lymph nodes. Tuberculosis seems to show a predilection for these glands which form a portal of entry past the barriers of cartilage, muscle and elastic tissue. Although direct implantation from sputum can occur, it is rare because of the protective action of cilia, mucus and bronchial peristalsis.

These lesions appear to occur chiefly as a complication of far advanced pulmonary tuberculosis. Some cases develop fairly extensive tracheobronchial lesions while the parenchymal involvement is moderate in extent and even shows evidences of healing. Some of these lesions heal spontaneously but many patients

with this complication fail rapidly unless the bronchial involvement is recognized and treated.

Wheeze is the most frequent and most reliable symptom of a tuberculous tracheobronchial lesion. It is not transitory, though varying in intensity, but persists over days, weeks or months. The wheeze persists after expectoration, is loudest over the site of the lesion, and often transmits marked vibrations to the palpating hand It is usually most evident in the parasternal regions. The wheeze may only be produced on exertion or forced expiration, thus being missed during quiet breathing. To elicit this sign, the patient is requested to take a deep breath and then exhale forcibly, while the stethoscope is applied to the parasternal regions. If pneumothorax is present, the wheeze may sometimes best be heard by placing the stethoscope over the suprasternal notch as the sounds are transmitted up the trachea. To make a clinical diagnosis, it is important to make repeated daily stethoscopic examinations, particularly after the patient has expectorated as completely as possible

Dyspnea, when out of proportion to the patient's other findings, is a suspicious symptom. A sense of obstruction often accompanies the dyspnea

Positive sputum persisting after obtaining good collapse of the diseased area always should suggest the presence of a tracheobronchial lesion, particularly when accompanied by periods of fever and sputum block with resulting marked variations in amount of expectoration. Difficulty in raising sputum is suggestive.

Continuous or intermittent atelectasis of one or more lobes is a definite indication of bronchial obstruction and, therefore, of a bronchial lesion. During the periods of atelectasis the wheeze may disappear because of the complete bron-

chial block, and recur when a partial lumen is again established

Treatment—The high frequency electrocoagulating current applied by means of the Kernan electrode through either a 5, 6, or 7 mm. bronchoscope has been used for treatment of tuberculous lesions of the bronchial mucosa. The strength of the current used should be of low intensity so as to minimize the possibility of producing necrosis of cartilage in the bronchial wall. Accurate standardization of current is probably not important because the effectiveness of coagulation at a given point for a given strength will vary, depending upon the amount of mucus or other exudate between the electrode and the diseased tissues. The current control is kept at its lowest point unless a mass of tissue projecting into the bronchial lumen is to be destroyed The length of time that the electrode is applied at any 1 point varies from 1 to 5 seconds, avoiding producing coagulation deeper than 1 mm. This treatment is not an attempt to destroy all of the tuberculous tissue present, but to stimulate the reparative processes of nature

Cauterization of tuberculous laryngeal lesions has been an accepted form of treatment for many years. Electrocoagulation has the same physiological effect as the actual cautery, namely, the production of a burn. This is beneficial because it induces hyperenna and hastens fibrosis, stimulating the natural tissue response.

The lesions spread by continuity along the submucosa, originating in most cases in the bronchus, draining the affected lobe and spreading outward into the next larger bronchus. Since a treatment is available that induces healing in small ulcers, it is important than an early diagnosis be made and treatment instituted before the ulcer has had time to involve the entire circumference of a

major bronchus. It is obvious that there will be less scarring and contraction from healing of a small ulcer than there will be from healing of a large one. If the treatments are gently carried out and normal mucosa is not burned or traumatized, there will not be any more cicatricial stenosis than would develop if spontaneous healing would occur.

Mechanical dilatation of fibrous strictures has not been effective except for very temporary relief of sputum retention

Cicatricial stenosis of marked degree is still a serious problem for which lobectomy may eventually prove to be the solution. Cautery excision of these severe stenoses involves a very real danger of perforation of the bronchial wall.

Over a period of 20 months, 8 patients have been treated by electrocoagulation current of weak intensity. Treatments were given at intervals of 2 to 4 weeks. A total of 84 treatments were given No harmful effects were noted as a result of the bronchoscopic treatment and in each case the tracheobronchial lesions showed a consistent tendency to heal There were no lary ngeal complications and no spread of the parenchymal lesions

Five patients are chincally well. Two of these show complete healing of their tracheobronchial lesions but still show occasional positive sputum. Two patients are improving satisfactorily under treatment. Treatments were discontinued in 1 case because of the patient's extreme debility and emaciation. The patient longest under treatment has had no recurrence of positive sputum or wheeze in the year following healing of her tracheobronchial lesion.

Diagnosis—Epituberculosis—W.B. Wood³¹ believes that epituberculosis is a manifestation of postprimary tuberculosis in childhood and occurs in a period characterized by enlargement of the

bronchial glands and a tendency to exudation.

The chief factor in its production is atelectasis due to bronchial blockage by tuberculous glands. A secondary factor is probably exudation into the alveoli and engorgement, the result of lymph stasis and vascular congestion. Tuberculous allergy possibly also plays a part for allergic reactions are common in the second stage.

If gland caseation leads to rupture of the wall of a bronchus, a caseous bronchitis or bronchopneumonia may entirely alter the clinical picture and cause permanent damage to the lung. If the bronchial wall escapes such ulceration, restitution can occur and the collapsed lobe may return to its original condition. A failure to re-expand must in either event give rise to bronchiectasis, which is a common result of tuberculous adenitis.

One cause of the hilus flare phenomenon is atelectasis of the right middle lobe due to bronchial compression. Collapse of the apical division of the lower lobe may cause a similar shadow and have a comparable origin. Many of the triangular shadows on the hilus are evidently due to a local atelectasis. Care is needed in their interpretation because other lesions of a tuberculous and nontuberculous nature may cause similar opacities.

The term "epituberculosis," which has served its purpose and drawn attention to the condition, might now be abandoned.

Case Finding—J. R Pastor³² of the Department of Health, San Juan, Puerto Rico, states that the public health procedure of tuberculosis case finding in Puerto Rico consists of fluoroscopic examinations complemented by x-ray plates of suspicious or positive cases. In Puerto Rico, every medical health officer is being trained in the use of the fluoroscope.

There is some fear of the fluoroscope among general practitioners because of an exaggerated notion of the harm that may come from its frequent use. The modern fluoroscopic apparatus is so well protected that the danger from an overdose of x-rays through its use is practically negligible. There is need of an educational campaign among physicians in this respect. No medical office should be without this indispensable diagnostic equipment. A more extensive use of the fluoroscope by the general practitioner could be an immense help in the fight against tuberculosis.

The slogan "Use the fluoroscope more!" should become universal among tuberculosis workers.

Tuberculin Patch Test—H. Vollmer and E. W. Goldberger³³ made a comparative study on 678 children to determine whether or not their patch test can be safely substituted for the Mantoux test.

None of the children who showed a positive reaction to the Mantoux test with 0.1 mg. of old tuberculin, failed to react simultaneously to the patch test. There were even more positive reactors to the patch test than to the Mantoux test. Therefore, it seems that the Mantoux test can be replaced by the tuberculin patch test, at least as the first test. Higher concentrations of tuberculin must later be applied intracutaneously in order to rule out completely any tuberculous infection.

The patch test might be preferable to the Mantoux test as the first diagnostic measure. The disagreeable local, focal and constitutional reactions that occasionally result from the Mantoux test did not follow the patch test.

The following is a suggested procedure for tuberculin testing.

1 The tuberculin patch test is applied and read 2 days after the patches are removed.

- 2. Negative reactors to the patch test are retested with the Mantoux test with 1 mg. (0.1 cc. of a 1:100 solution) of old tuberculin or second strength solution (0.005 mg.) of purified protein derivative.
- 3. Since higher concentrations of tuberculin occasionally cause pseudopositive reactions, both tests are repeated if there is any discrepancy. If the discrepancy remains, the Mantoux reaction is regarded as the deciding one.

Repeated Tuberculin Tests—J. R. Forbes³⁴ reports that normal subjects, who were given intracutaneous tuberculin tests at intervals of 1, 2, 3, 4 and 6 week intervals, show the almost constant occurrence of supersensitation after the first test when the test is repeated at intervals of less than 3 weeks.

After this early increase, sensitivity tends to decline gradually under the influence of frequent repeated testing. However, the results are by no means uniform and unexpected variations of sensitivity are common.

Because of the considerable variability of sensitivity in normal subjects as shown by repeated tuberculin tests, great caution must be observed in attempting to relate the results of such tests to the course of the disease in tuberculous patients.

Comparison of Intermediate and the 2-Dose Tuberculin Tests — R. I. Canuteson³⁵ tuberculin tested 4108 students over a period of 3 years.

An average of 16 94 per cent of positive reactors was isolated with a single intermediate dose and 40 1 per cent with the regular 2-dose test. The incidence of the adult type of tuberculosis was 0.512 per cent with the intermediate dose and 0.609 per cent by the regular 2-dose method. There were no plus 4 reactions with the small intermediate dose of 0.0002 mg. The incidence of 4 plus reactions with the large intermediate dose of 0.0005 mg. was 1 004 per

cent and with the routine 2-dose test it was 0.355 per cent.

Retesting the negative reactors to the large intermediate dose with the regular second dose, increased the positive reactors in a group of 735 students from 15.37 per cent to 35.51 per cent and the incidence of secondary tuberculosis from 0.54 per cent to 0.68 per cent, representing 1 additional inactive case.

The incidence of secondary tuberculosis determined by use of the smaller intermediate dose of 0.0002 mg. was 0.508 per cent and by the larger intermediate dose of 0.0005 mg was 0.515 per cent

Value of Intradermal Tuberculin Test—D B Bradshaw³⁶ performed 3010 intradermal tuberculin tests, using 1 1000 tuberculin. The diagnostic value of the test has been found to be underrated, especially in older children. The test enables a diagnosis of tuberculosis to be excluded in 3 out of 4 "suspected cases" in children up to 8 years of age and in one-half of those from 10 to 12 years of age.

Evaluation of Different Technics in Obtaining Gastric Specimens for Examination for the Presence of Tubercle Bacilli—(1) A Lassman³⁷ used a technic different from that used by Neumer to collect the gastric contents of patients having, or suspected of having pulmonary tuberculosis

All specimens are collected the first thing in the morning or as near the waking time of the patient as possible. Both ambulatory and nonambulatory patients are given the same preparatory instructions.

1 Complete restriction of all foods and fluids after 7 P M the night before, until the gastric contents have been obtained. Infraction of this rule interferes with the proper evaluation of the findings.

2. On awakening, the patient is not allowed to brush his teeth, rinse his mouth, nor drink a drop of water, prior to having his stomach contents aspirated. In this manner, a concentrated accumulation of everything the patient has swallowed during his sleep, plus any infective material that may be present in the stomach, is obtained.

In all bed patients, the stomach contents are obtained on awakening or within 10 to 15 minutes at most

The ambulatory patient is requested by special appointment to appear as soon as possible after he awakens, in order to aspirate as much of the accumulated infective material as possible. The regulation stomach tube is not used nor is any tepid water injected while in the process of getting the stomach contents, thus getting an undiluted and concentrated specimen to examine

A Lavine or Rehfuss tube is passed into the stomach, and with a Luer syringe 1 to $1\frac{2}{3}$ oz (30 to 50 cc) of the concentrated gastric contents are aspirated, for examination for tubercle A specimen obtained by this method will give a better evaluation of actual conditions present, than a diluted one obtained by the older method. No matter how few bacilli may be present, the very fact that the gastric contents are undiluted, assures the finding of the germ in a greater percentage of cases, whereas, if there are few tubercle bacilli present in the stomach contents, then, by diluting the specimen, it naturally is more difficult to prove their presence and they may be overlooked entirely.

All specimens obtained were examined by the slide method and if found negative, then by culture growth and guinea pig inoculation

The specimens collected by the older method, using $3\frac{1}{3}$ oz (100 cc) of tepid water as a diluent, showed a 12 per cent

positive finding of the tubercle bacilli. The specimens collected by the new, more concentrated method, showed a 20 per cent positive finding of the tubercle bacilli.

Giant Cavities—P. N. Coryllos and G. G. Ornstein³⁸ state there are 2 varieties of giant cavities, tension cavities containing positive pressures of air, and cavities with atmospheric pressures.

The tension cavities are always spherical. They correspond to the variety known as ballooning, check or ball valve cavities. Their walls are thin and fluid is often present in them. The general condition of the patient is rather good and the sputum is often negative. These cavities may disappear spontaneously and reappear periodically at the same place and with the same characteristics. Lipiodol and dyes injected through the chest wall remain in them for a variable length of time but are finally expectorated.

Cavities with pressures equal to the atmospheric pressure show no accumulation of fluid, do not disappear spontaneously, and present unyielding resistance to collapse therapy. Their walls are more frequently thick and the sputum is persistently positive. Lipiodol and dyes injected into them are immediately or very rapidly expectorated. They are chronic, progressive cavities that increase in size gradually and steadily by continuous sloughing of the pulmonary parenchyma.

All giant cavities are open cavities. In a number of them, a valve mechanism is formed in their narrowed bronchus causing its intermittent and partial closure, leading to the formation of positive pressure in these cavities (tension giant cavities). In others, however, the draining bronchus remains open (open giant cavities).

All tuberculous cavities ought to be distinguished as open (continuously or

intermittently) and closed cavities. The closed cavities are those which shrink and disappear if the nature of their walls allow it; but even when they cannot shrink, they may heal biologically (cavities with smooth walls) even when they remain visible in the x-ray films. Open cavities remain active unless their bronchi become completely and definitely obliterated, when they change to closed cavities.

The draining bronchus of a tuberculous cavity has an important effect on the evolution of the cavity. Only wide patency of the draining bronchus can explain atmospheric pressure in the cavity, absence of retention, and positive sputum

Partial obstruction of the bronchus with valve action, allowing ingress of air during inspiration but not free egress during expiration, can explain positive pressure in the cavity, retention of exudate or of fluid injected into it through the chest wall and negative sputum. Narrowing of the draining bronchus causes ballooning of the cavity by the mechanism of obstructive emphysema. That these cavities remain open indicates that this obstruction is only partial and transient.

Definite obstruction of the draining bronchus causes disappearance of cavities by the mechanism of obstructive atelectasis and if the obstruction is complete, positive pressure in the cavity is not possible

Classification of cavities has also been based upon the characters of the walls but they also vary according to the degree of patency of draining bronchi. Patent bronchi allow free circulation of air into the cavities with an adequate amount of oxygen which is necessary for the growth and metabolism of the strictly aerobic human tubercle bacilli. Under these favorable conditions of growth and

metabolic activity of tubercle bacilli, tuberculin is produced freely, causing increased tissue sensitivity and consequently perifocal reaction and infection, and thickening of the walls of the cavities.

Prognosis—The percentage of cures of giant tuberculous cavities is actually very low.

Treatment - Pneumothorax and thoracoplasty should be tried first in the management of giant tuberculous cavities of the lung. The success of the pneumothorax is dependent to some degree on the extensive adhesions of the cavity to the chest wall and on the thickness of its walls However, the draining bronchus is the most important factor in their closure. Closure has not been obtained when the draining bronchus is wide open and of rather large diameter. As long as the draining bronchus is open, the cavity not only resists all attempts at collapse (pneumothorax and even thoracoplasty) but may expand under the collapsed chest wall.

Cavities, apparently fibrotic and adherent to the chest wall, often respond to pneumothorax and satisfactory selective collapse may be obtained or can be completed by pneumonolysis. Likewise, very large giant cavities with very thick walls, and apparently hopeless, have responded well to thoracoplasty.

Closed pneumonolysis, when possible, however, has given a number of satisfactory closures, though it sometimes has failed or even caused greater expansion of the cavity.

Crushing of the phrenic nerve or exeresis has not given satisfactory results.

Thoracoplasty with wide apicolysis is the procedure of choice when pneumothorax and pneumonolysis have failed.

In 43 patients, revisions of thoracoplasties with resection of the regenerated bone have given a 29 per cent good result. Extensive anterolateral thoracoplasties have not been any more successful.

When the apex can be stripped from the chest wall, lowered down, and anchored in this position, either by sutures or by placing above it a muscular flap at the place previously occupied by the apex, good results are more likely. Unfortunately, it is not often possible to strip the uncollapsed cavity from the regenerated ribs. The uncollapsed cavities are usually much larger than they appear on the x-ray film and their separation from the chest wall or the lung from the parietal pleura is often impossible without tearing them.

In 2 cases, lobectomy was tried. In 1 case the upper lobe was removed, after a 3-stage thoracoplasty did not succeed in closing a giant open cavity. The upper lobe was separated from the parietal pleura and removed. Careful closure of the bronchus was done. A bronchial fistula developed 10 days after operation and the patient died 5 months later with extension of the disease. Efforts to close the fistula were unsuccessful.

The second patient had 2 giant open cavities, 1 in the upper and 1 in the lower right lobe. Pneumothorax could not be induced Three-stage thoracoplasty and phrenicectomy did not succeed in closing either of the cavities. During reoperation the lower lobe, which contained the larger cavity, was separated from the parietal pleura The vessels of the pedicles of the lower and middle lobes were tied and sectioned, and the bronchus was sectioned, carbolized and sutured Sputum became negative after operation A bronchial fistula developed the sixteenth The patient died 2 months later with symptoms of amyloid nephrosis. The bronchial fistula did not close up till the time of death but the sputum remained negative

Collapse procedures have not given satisfactory results. Closure of the draining bronchus should bring about healing of the cavity or at least render the sputum negative.

W. D. W. Brooks³⁹ reported a good result obtained by obstructing the lower right lobe which contained a large cavity, for 6 hours by means of a rubber balloon. In this case, however, pneumothorax was present in the right pleural cavity.

Closure of the lobar bronchus of the affected lobe has not been attempted because of the danger of suppurative pneumonitis of this lobe. Frequently, pyogenic organisms are present in the large bronchi of these patients.

In 6 cases, intracavitary transthoracic attempts were made to obliterate the draining bronchus. After accurate localization of the cavity, a needle was introduced into it through the chest wall When it was certain that the needle was in the cavity, 1 of the following substances were injected into the cavity: Solution of copper morrhuate; blood taken from the patient (simple or mixed with thrombin in order to produce rapid coagulation), silver nitrate (30 to 60 per cent solution), aseptic gelatine (8 per cent previously heated), or agar (15 per cent heated to 40° C.) No satisfactory results were obtained by these procedures. There were no untoward effects following these injections.

In 3 other cases, the cavernoscope was used In 1 of the cases, a few drops of a 60 per cent solution of silver nitrate were injected directly into the orifices of the draining bronchus In the second case, the mucosa of the draining bronchus was cauterized by means of a fine galvanocauteric knife introduced through a second cannula The cauterization was carried out under the control of the cavernoscope as in closed pneumonolysis.

In the third case, monolate (the sclerogenic solution used for injection of hernias) was injected around the orifice of the draining bronchus. The procedures were unsuccessful. No bronchial closure was obtained.

In 12 cases, a procedure of opening the cavity and filling it with a pedunculated muscular flap gave a 50 per cent negative sputum conversion, but the procedure is fraught with dangerous complications.

The technic is as follows: An incision is made on the scar of previous thoracoplasty and the regenerated bony plate is excised. The parietal pleura is excised and the flaps dissected bluntly from the lung. By palpation, the cavity is easily located and its presence is made certain by puncturing it. Air and pus are aspirated. Then the cavity is widely incised. In all the cases operated, there was blowing through the draining bronchus although the orifice of the latter could not always be visualized The size of these cavities varied from that of a large walnut to an orange. Methylene blue introduced into the cavity was expectorated in all the cases The cavity was then carefully and gently sponged until perfectly dry A long pedunculated muscular flap is raised from the paravertebral muscles and turned into the cavity so that it fills it completely, and is fixed in this position with interrupted stitches of catgut The parietal pleura is closed above the flap and the wound closed in 3 layers. In 4 of the 12 cases treated, a small rubber dam was placed in the upper end of the wound In 8 of the cases the wound was closed without drainage after bacteriologic examination of the purulent cavity contents had shown that no pyogenic organisms were present.

The immediate results in the 12 cases operated were very satisfactory. There was no mortality as a result of the opera-

tion, although the procedure was long and laborious, and in all these patients, the cases were of long standing, presenting advanced amyloidosis, and all other methods had failed to close the cavities and to convert the sputum. The wound closed by primary healing in all but 2 of the patients. However, there was secondary opening between 10 and 20 days after operation, and serohematic fluid was eliminated.

Of these 12 cases, 6 became sputumnegative immediately or shortly after the operation One of these became sputumpositive again a month later

Four of the 12 patients died The first died 3 weeks after operation with acute bronchial obstruction, the second with uremia due to amyloid nephrosis (a case of advanced amyloidosis with 100 per cent absorption of Congo red before having been operated), the third (a bilateral case with pneumothorax on the other side) developed spontaneous contralateral pneumothorax and was deflated with marked relief but died with bronchopneumonia in the contralateral side The fourth patient became persistently negative 2 weeks after operation and was ambulatory for 4 months. He contracted pneumococcic pneumonia in the contralateral lung and died.

Autopsy findings of the patients who died from 3 weeks to 4 months after operation disclosed that during the first 3 postoperative weeks, active tuberculization of the muscular flap took place. On the patient who died 3 weeks after operation, the flap was in place and no tuberculization could be seen. It was adherent to the cavity by fibrin but could be easily detached. The patient who died 4 weeks after operation had extensive tuberculization of the flap Caseated tubercles were found in it, and it was filling the cavity and was adherent to its walls. The fourth patient, who died 4

months after operation, became sputumnegative shortly after the operation and had remained such. Autopsy revealed the flap was in place, was completely adherent to the walls of the cavity and was transformed into fibrous tissue. The draining bronchus of the cavity was closed. The flap had completely obliterated the cavity. The right lung was completely consolidated by pneumonococcic lobar pneumonia. This patient had had positive sputum for 4 years after complete thoracoplasty and 2 revisions.

Thus, while the procedure is effective, it is followed by tuberculization of the flap.

Endobronchial Tracheobron-Оľ chial Tuberculosis — Treatment — B. Goldberg⁴⁰ states that the usual therapeutic tuberculosis régime should be closely followed. Bronchoscopic aspiration of thick tenacious mucus which may cause a temporary bronchial occlusion and atelectasis, may be practiced Topical application of epinephrine, 1/1000, or cocaine, 10 per cent, may allow temporary shrinkage in the presence of edema Silver nitrate in solution of 10 per cent to 30 per cent may be applied topically through a bronchoscope in the forms where the hyperplastic type predominates or where the ulcerative type is not completely annular.

Electrocautery has been used in some localized lesions with success Roentgen therapy may be of value in some patients where the annular type circumventing the bronchus is not present, because of stimulation to scar tissue formation, and obstruction Dilatation of stenotic lesions with fine bougies has been practiced but there is danger of rapid spread into the parenchyma and possible miliary tuberculosis where mucosal infiltration or ulceration exists

Artificial pneumothorax has been tried, not as a curative measure, but in

the hope of preventing parenchymal spread and disease. *Tracheotomy* has been necessary in the presence of acute edema as an emergency measure.

Pulmonary Tuberculosis Following Serofibrinous Pleurisy—L Schneider⁴¹ believes that acute pleurisy with effusion uncomplicated by pulmonary lesions should be considered of tuberculous origin in nearly every case, and like pulmonary tuberculosis, the majority of these cases occur in youth and early maturity

In a typical instance, the patient is acutely ill for several weeks or a month or 2 but almost always recovers his health, at least temporarily, on the absorption of the fluid. It is safe to conclude that the sudden occurrence of an effusion in a young person who has been previously well, and which cannot be attributed to pneumonia, infarct, rheumatic fever, blood dyscrasias, the congestion of heart disease or the transudation in kidney disease, is undoubtedly due to tuberculosis whether tubercle bacilli are or are not found in the fluid

Although it is believed that the most dangerous period after pleurisy is the 5 years immediately following, pulmonary tuberculosis developed in 2 patients 7 years after the effusion, and has also been diagnosed 11, 12, 14, and 16 years later The mortality from the later pulmonary disease is from 20 to 25 per cent. Kallner has reported 605 pulmonary tuberculosis patients, of whom 19 per cent had pleurisy before pulmonary tuberculosis developed Fishberg states that between one-third and one-half of the pulmonary tuberculosis patients have had pleurisy before symptoms referable to their lungs manifested themselves

The present concept of aftertreatment of so-called idiopathic pleurisy may have to be changed to prevent future needlessly high tuberculous morbidity. **Arti-**

ficial pneumothorax should be instituted on the side affected by the pleurisy and maintained for a number of years if possible as a means of preventing the subsequent development of pulmonary tuberculosis, which almost invariably affects the lung underlying the effusion.

Every case of pleurisy should be considered one of potential tuberculosis unless some other cause for the effusion is found. These patients should receive the same repeated observations, from the public health standpoint, as those with pulmonary tuberculosis

Relationship of Bone and Joint Tuberculosis to Pulmonary Tuberculosis — H Frank, 42 after investigating the relationship between bone and joint tuberculosis and pulmonary tuberculosis in 1003 patients treated at the sanatorium of Heuberg, found that the simultaneous existence of pulmonary tuberculosis and bone and joint tuberculosis in infants and children, is frequent. This is explained on the basis of the frequency and the regularity with which infection and reinfection take place at that age, as well as on the feeble resistance of young bodies

Simultaneous pulmonary involvement is equally frequent in somewhat older children, most of whom exhibit advancing ulcerative pulmonary tuberculosis Simultaneous involvement of the pulmonary tissue between the ages of 10 and 30 years is rare. The fact that most of the cases of bone and joint tuberculosis occur at this age suggests the possibility of the existence of isolated chronic tuberculosis of a single system.

A spreading ulcerative pulmonary tuberculosis occurred in 2.4 per cent of all cases of joint-bone tuberculosis. The rest of the cases of pulmonary involvement presented benign forms of the disease, which is explainable by the exis-

tence of positive allergy of the body in bone and joint tuberculosis.

The coexistence of pulmonary tuberculosis is not a contraindication to operative treatment of bone foci. Frequently, the removal of a tuberculous focus exerts a beneficent effect on the entire organism.

Treatment—P. D. Crimm and D. M. Short⁴³ point out that the average liver content of vitamin A of 50 tuberculous patients (342 units per Gm. of liver) compares favorably with that reported (331 units) previously for healthy persons. This, however, is far from the saturation point as evidenced by the wide variation between it and individual cases.

The average is about one-fifth of the maximal finding (1640 units). The distribution according to age is not significant, except for the fact that in older persons the vitamin A content is somewhat increased. The abundant nutrition given tuberculous patients and the prolonged duration of the fibrotic disease would account for these results.

The vitamin A content of the human liver approached depletion in 14 per cent of the patients. All patients with enteritis had values below the average. Therefore, the administration of generous doses of *vitamin A* is indicated in tuberculosis with pyrexia or enteritis.

- R. K. Childerhose⁴⁴ states that the purposes of *pneumothorax* are as follows:
- 1 Relaxation of the affected portion of the lung so as to hasten fibrosis
- 2. Reduction of toxemia by the occlusion, partial or complete, of the lymphatics draining the lesion.
 - 3 Closure of cavities.
 - 4 Prevention of spread.
 - 5. Cessation of hemorrhage.

Indications for *pneumoperitoneum* are slightly different from those for pneumothorax. It has been noted that

a rise of the diaphragm in the absence of myocardial disease has a beneficial effect on the breathing of patients with emphysema. In cases of basal tuberculosis it is of definite help and in those in whom a phrenic nerve interruption has been done, a pneumoperitoneum will greatly increase the clinical benefits by raising the diaphragm still more.

Occasionally, a patient whose condition is not sufficiently good to warrant a thoracoplasty may be improved by pneumoperitoneum to such an extent that the operation can then be performed.

It has been noted that tuberculous activity is not as apparent in pregnancy as it is after delivery. This has been attributed to the elevation of the diaphragm during pregnancy. The subsequent increased activity after delivery is due to the greater movements of the diaphragm later. Pneumoperitoneum is indicated in these patients following their confinement.

The advantages of pneumoperitoneum are the ease with which it can be carried on and, when necessary, be discontinued. There is no awkward belt to be worn and there is no interference with the nerve supply to the diaphragm.

M. Canizares⁴⁵ states that since the advent of the x-rays and the tuberculin test, early detection of tuberculosis of the lungs has been made relatively easy. Such a case, once detected, should be placed under the closest observation so that artificial pneumothorax or some other form of collapse therapy, aided by rest and proper regimen, can be instituted at the very first sign of disease activation

Judicious use of collapse therapy at an early stage of the disease:

- 1. Prevents the dangers of pulmonary hemorrhage.
- 2 Checks bronchogenic spread of bacilliladen sputa.

- 3. Prevents lymphogenic seeding of the disease, not only to the lungs, but to the intestines, the kidneys, the larynx, the peritoneum and the meninges as well.
 - 4 Closes pulmonary cavities.
- 5. Excites fibrosis by production of local anoxemia
- 6. Provides for effective pulmonary compression by avoidance of pleural changes.

At the hands of trained phthisiologists or thoracic surgeons, collapse therapy has proven itself the most powerful weapon against pulmonary tuberculosis: as well as the short-cut to the incapacitated patient's rehabilitation. In this manner, the conversion of sputum and subsequent arrest of the tuberculous process is hastened, the tuberculous breadwinner is returned to his earning capacity within the shortest period, and he ceases to be a source of infection and a liability to his family as well as a social and epidemiological problem to the State.

Prophylaxis of Tuberculous Empyema—L Roberts⁴⁶ reports that the incidence of tuberculous empyema in patients with artificial pneumothorax is about 10 per cent and its fatality rate is about 50 per cent

Prevention seems especially important Persistent or recurrent pleural pain over the lesion indicates severe tuberculosis of the pleura, which contraindicates artificial pneumothorax

The risk of empyema is sufficiently great to make some other form of collapse therapy advisable. The object of artificial pneumothorax is relaxation, not compression, of the lung High positive pressures to "stretch the adhesions" are not justifiable.

After adhesions have been cauterized and collapse has been instituted, a pneumothorax which remains ineffective should be promptly abandoned and other collapse therapy substituted.

Oleothorax and extrapleural pneumothorax are valuable in certain cases.

Permanent Results of Collapse Therapy—G. Bucholdt⁴⁷ in 1937, made a follow-up of patients with pulmonary tuberculosis who received collapse therapy (exclusive of thoracoplasty) at the clinic in Jena during the years from 1925 to 1935, that is from 2 to 12 years after the beginning of the collapse therapy.

Collapse therapy had been carried out in 297 cases. In 76 others, it was not employed, although it was indicated, either because the patients did not consent to it or because collapse could not be induced on account of pleural adhesions.

Of the cases who had received unilateral pneumothorax, 48.5 per cent were free of bacilli from 2 to 12 years after the collapse therapy. Of the bilaterally treated cases, 21 per cent were free of bacilli.

There were indications that favorable therapeutic results are to a great extent dependent on the long duration of the pneumothorax therapy. The therapeutic results were most favorable in the patients between 20 and 25 years of age but they were not much less so up to the age of 45.

Freedom from bacilli was obtained in only 21 per cent of the cases in which pneumothorax was not induced, although the indications for treatment were the same as those treated unilaterally in whom 48.5 per cent became bacilli free. Thus, if in a group of patients with pulmonary tuberculosis, 100 are cured spontaneously, 230 could be cured by collapse therapy.

Re-establishment of Pneumothorax—A. Rest⁴⁸ reports that of 135 collected cases in which an attempt was made to re-establish pneumothorax, in 52 of these it was re-established successfully. Of the 52 successful cases there

were adhesions in 40, there was none in 7, and this was undetermined in 5.

The period of time for which pneumothorax was maintained before it was discontinued varied from less than 1 year in 21 cases to more than 6 years in 1 case. Some of the reasons for discontinuing pneumothorax in these 52 cases were obliterative pleuritis, poor collapse, discontinued by patient, adequate collapse at the time and contralateral spread. The reasons for re-establishing the pneumothorax were that some of the patients had reactivation, inadequate collapse, an increase in symptoms, to replace effusion, positive sputum or hemoptyses.

Re-establishment of pneumothorax is possible more often than was formerly believed and should always be tried when further compression is desired. The long duration of a pneumothorax and the interval after a pneumothorax was abandoned, are not contraindications for reestablishment. Re-establishment of pneumothorax, although possible, is far from a general attainment. Consequently, as pulmonary tuberculosis is characterized frequently by relapse, it seems plausible to continue pneumothorax indefinitely and to consider its abandonment with reluctance.

Pneumoperitoneum—H G Trimble, J L Eaton, and G Moore, 49 during the years 1934 to 1937, used pneumoperitoneum in the treatment of pulmonary tuberculosis on 152 patients, with distinct benefit in many instances

Pneumoperitoneum is recognized as 1 of the various collapse procedures available in the treatment of pulmonary tuberculosis and many patients are receiving air intraperitoneally. A definite rise in the diaphragm can be obtained and a marked splinting occurs. When associated with an operation on the phrenic nerve, a marked rise of the paralyzed hemidiaphragm, at times to the

level of the second rib anteriorly, often results.

The procedure is of value in patients in whom pneumothorax has failed, either because of mability to find any free pleural space or because only a small ineffective collapse could be obtained, and in which for various reasons more drastic types of collapse therapy are not indicated at the time A phrenic crushing plus pneumoperitoneum is often the next logical step in treatment. This may bring the disease to a point where surgery is possible, or may even bring about an arrest Pneumoperitoneum is indicated in patients with pulmonary tuberculosis having extensive far advanced bilateral lesions still in the exudative stage, in which no other form of collapse therapy is advisable

The procedure, in the absence of chronic myocardial disease, gives rise to little or no dyspinea. In cases complicated by a compensatory emphysema, the effect is often beneficial and respirations are facilitated. Pneumoperitoneum has been used with improvement in a few cases of pulmonary emphysema uncomplicated by tuberculosis.

After the first several refills, very few of the patients experience any discomfort Gastrointestinal symptoms have not been of great moment. Occasionally, ascites has been observed, which may come and go, and, except in the presence of a tuberculous peritonitis, needs no treatment. There is a striking similarity in the behavior of this fluid to the pleural effusions so often noted during pneumothorax Tuberculous peritonitis has not occurred more often than the normal expectancy In a few cases an adhesive peritonitis has developed which has made it impossible to continue the refills, again paralleling the adhesive pleuritis that at times develops during pneumothorax therapy

To determine more specifically the effect of long continued air and pressure on the peritoneum and abdominal viscera, the autoptic and microscopical findings on 20 patients treated by pneumoperitoneum were studied.

All of the 20 patients had far advanced pulmonary tuberculosis and all but one had bilateral disease. The prognosis was considered as unfavorable in all cases. A third of the group had extrapulmonary tuberculous complications and one case was complicated by syphilis. The ages varied from 15 to 59 years, 2 being under 20 and 4 over 50 years of age.

The length of time during which pneumoperitoneum was continued varied from 1 to 33 months, 6 having received it from 1 to 3 months, 5 from 4 to 6 months, 3 from 7 to 12 months, 4 from 13 to 24 months, and 2 from 25 to 33 months. In all cases enough air was given to obtain a good rise of the diaphragm. Other collapse therapy (pneumothorax, phrenic nerve operation, wax apicolysis, thoracoplasty) was used or attempted in combination with pneumoperitoneum in 28 instances.

Thoracolysis—L O'Shaughnessy and Mason⁵⁰ used the procedure of thoracolysis in 8 cases of tuberculosis in which the disease, usually fibrocavernous, has involved mainly the middle or lower zone of 1 lung, and in which it has been impossible to obtain an adequate collapse by artificial pneumothorax, and in which healing has not followed diaphragmatic paralysis. For this type of case, the alternative to thoracolysis was a "total" thoracoplasty with the consequent functional sacrifice of an unduly large area of healthy lung tissue. This was considered an operation of undesirable severity in view of the general condition of the patients.

Thoracolysis consists essentially of making the chest wall more yielding in

some desired situation and so permits retraction of any scar tissue in the underlying lung. Healing was started by carefully designed selective resections of relatively small portions of the ribs in the vicinity of the lesions, just where relaxation of scar tissue of the underlying lung was required.

The portions of ribs which it is usually necessary to remove in this operation are easily accessible through direction incisions and tissue trauma is reduced to a minimum as little retraction is necessary.

Consequently, the operation is one which can be employed for patients in relatively poor physical condition. It is a comparatively easy operation to carry out under local anesthesia, should this be desirable. The cases operated were comparatively free from marked post-operative disturbances.

If there is clinical and radiological evidence that the operation has favorably influenced the lesion, but has not healed it by the time the ribs have regenerated, the operation may be repeated

Partial Thoracoplasty Without Deformation—M. Iselin and C R. Arp⁵¹ state that the deformity resulting from a routine thoracoplasty is due to 3 causes:

- 1 Vertical lowering of the scapula with subsequent fall of the shoulder.
- 2. Sinking of the scapula into the depth and its lateral projection.
- 3. Scolosis, with convexity toward the side on which operation was done.

From the orthopedic point of view, the removal of the transverse processes of the vertebrae is a mistake. To cause no deformity, thoracoplasty should not involve the trapezius muscle, the angular and rhomboid muscles or the latissimus dorsi muscle, since these muscles fix the scapula.

By modifying the direction of Picot's incision and cutting some of the trapezius

fibers (the ascending fibers which play no part in fixation of the shoulder), it is possible to perform thoracoplasties involving as many as 6 ribs and to perform extrafascial apicolysis under conditions far more favorable than those obtained in making the usual incisions around the scapula

The cutaneous incision is oblique, starting at the seventh cervical vertebra (the prominent one) and extending as far as 3 cm. below the angle of the scapula. The upper part of the incision does not have to reach the seventh cervical vertebra but starts 1 cm. from it and, if necessary, its lower extremity may be prolonged along the spinal border of the scapula. This incision allows a favorable approach to the most difficult point in surgical treatment of pulmonary tuberculosis, ablation of the first rib, the key of the thoracoplasty. With this incision, the ribs can be viewed one after the other

Extrafascial apicolysis is much more easily performed with this incision as the apex of the lung is exactly in the center of the wound

A set of instruments suitable for the operation is necessary. They consist of 2 Semb retractors, 2 strong double-bent retractors, 3 rugines, Brunner's costostome for costostomy and 2 spatulas of the type employed by Semb

The scapula can be easily retracted in spite of the preservation of its muscles. This is done by putting the patient flat on his stomach and raising the arm, which places the bone in the sagittal plane and entirely disclosed from the thorax. It is maintained in this position by means of a retractor.

This incision provokes little hemorrhage and, as the muscle is not cut, does not cause shock Reconstruction is simple, the ascending fibers of the trapezius muscle which have been cut must be carefully sutured. The dissociated mus-

cular parts are brought together by means of 2 sutures, as in McBurney's incision

Two years' experience with this incision in thoracoplasties and extrafascial apicolyses has shown excellent results.

End Results of Thoracoplasty— L. S. Peters and P. G. Cornish⁵² were only able to follow up 78 cases out of a series of 300 patients

Of 40 patients on whom complete thoracoplasties were done, 21 per cent became well (negative sputum and cavity closed), while 54 per cent are dead. All these patients were hopelessly ill and would ultimately have died had it not been for the surgical intervention. None was able to work even part time. The other 25 per cent are living with positive sputum and open cavity, no better than before operation and will ultimately die of tuberculosis.

Of 38 patients on whom partial thoracoplastics were done, 50 per cent are well (cavity closed and sputum negative), 34 per cent are dead. The other 16 per cent are sputum-positive, have open cavitation and are unable to work. They, too, will no doubt die of tuberculosis, but had thoracoplasty not been done, all would have died of their disease.

The indications for thoracoplasty are about the same as for pneumothorax. All the patients reported well have been so for from 2 to 15 years.

All patients who must otherwise die of their tuberculosis should be given the benefit of thoracoplasty if they offer a fighting chance for recovery. To do less is to sacrifice lives that might otherwise be saved.

Extrapleural Pneumothorax — R Nissen⁵³ reports that Tuffier, in 1891, was the first to advocate extrapleural pneumolysis, for detachment of the lung from the thoracic wall in cases with pleural adhesions. Twenty years later, the

same method for collapsing the lung in pulmonary tuberculosis, was used. In 1913, Meyer perfected Tuffier's operation by including pneumothorax in the procedure as a routine. This was called "extrapleural pneumothorax"

In 1929, Meyer's procedure was used in the treatment of a case of tuberculosis of the apex of the lung, in which it was planned to do an apicolysis combined with partial thoracoplasty by resection of the upper ribs. The patient suffered a collapse when the apicolysis was completed and the thoracoplasty was not done. In order to maintain the apex of the lung in collapse, the apical cavity was repeatedly filled with air, as for pneumothorax therapy, and was maintained for 14 months. The patient made a good recovery

After that, extrapleural pneumothorax was employed in cases in which the usual method of pneumothorax was impossible because of adhesions and thoracoplasty was contraindicated by the patient's poor general condition

The procedure was first used in the treatment of tertiary cavities, but the method did not always give good results in this type of lesion In 1 case the cavity perforated a few weeks after operation and death resulted. In 2 cases there was hemorrhage with formation of a hematoma The ultimate result was favorable in 1 of these 2 cases, but in the other no demonstrable diminution of the cavity was obtained. In some of these cases, poor results were due to insufficient collapse of the lung. In others, the collapse was sufficient while the pneumothorax was maintained, but when no more air was insufflated, there was filling of the residual extrapleural cavity with exudate, requiring repeated punc-In 2 cases the exudate became infected If good results were obtained after discontinuance of the pneumothorax, the extrapleural cavity was obliterated. In such cases, the pulmonary cavities disappeared and the lesions in the opposite lung appeared to heal to such an extent that the patient became symptom free.

The principles of the treatment are the same as those of the "classical" method of pneumothorax, but a positive pressure must always be maintained. The collapse of the lung with extrapleural pneumothorax is limited to the site of the cavity and immediately surrounding area. According to the site of the cavity, either the paravertebral, the anterior, or the axillary route may be used for insufflation.

Extrapleural pneumothorax should be considered only when pneumothorax fails as a result of widespread adhesions, when the extent of these does not allow of plombage, or when the general condition or the state of the other lung does not permit of a thoracoplasty. Within these narrow limits, extrapleural pneumothorax is the only possible method of collapse therapy. It may be employed even though one cannot expect much from it, and the rare permanent results gain in value when one considers the hopeless fate of the patients for whom this form of therapy is recommended.

There is a doubtful indication for extrapleural pneumothorax in the case of recent cavities with delicate pleural adhesions when a thoracoplasty seems unsuitable on account of the risk of mediastinal flutter, and a plombe because of the likelihood of its slipping down. These cases are relatively rare. Extrapleural pneumothorax is performed in cases of this type only when a sufficient degree of pleural thickening can be assumed. Then it is replaced by thoracoplasty (apical thoracoplasty). Extrapleural pneumothorax in such a case plays

the part of a preparation for rib resection.

A stand should be taken against the present tendency to extend the indications for the use of extrapleural pneumothorax. The operation is an adventure into the unknown. It is an easy procedure for both doctor and patient but a variety of complications is possible, and great caution is advised.

Thoracoplasty, its various modifications, and plombage are superior to extrapleural pneumothorax. When it is possible to apply them, extrapleural pneumothorax should not be considered

Lobectomy and Pneumonectomy-J. C. Jones and F. S. Dolley⁵⁴ state that as certain cases of tuberculosis are cured only by a partial or total surgical removal of the diseased lung, pulmonary lobectomy and pneumonectomy should be used in the modern program of surgical collapse therapy. It is impossible to accomplish complete removal of the tuberculosis of the lungs by pneumonectomy and lobectomy but there is a place for such operations when the partial or complete removal of a tuberculous lung offers the patient his only chance of cure, and when the patient's general condition is apparently suitable for major surgery. For years, surgeons have been laboring under the false premise that a tuberculous lung should not be touched While this is true in the majority of cases, we should bear in mind the occasional exceptions to the rule.

In patients having frequent large hemorrhages which are not controlled by collapse with pneumothorax and phrenicectomy, a lobectomy is a far safer procedure than thoracoplasty By lobectomy the bleeding is controlled in 15 minutes. whereas in the interim between stages of thoracoplastay in these severe bleeders. fatal pneumonic contralateral spread of the disease often occurs.

A suppurating lung is not cured by thoracoplasty but is often made worse because of disturbance of the bronchial drainage. Toxicity is usually increased by the burden of any surgery except that removing the source of the toxicity. There is no point in trying to collapse a boggy, hard, indurated shell of a lung. In these cases, a lobectomy or pneumonectomy is certainly the procedure of choice.

When tuberculous cavities are present and have failed to close after extensive thoracoplasty, a lobectomy for the residual cavity should be given due consideration.

Another type of lesion that should be treated by lobectomy is an atelectatic, firmly contracted honeycombed lobe, with persistent positive sputum after thoracoplasty has been completed.

There is also the rare unilobar basilar tuberculous cavity which does not heal after the usual procedures of collapse therapy have been employed. Lobectomy should be considered in all such cases if the patients are good, or fair risks for major surgery.

Of 4 cases of tuberculosis, treated by lobectomy and pneumonectomy without mortality, 2 of the patients are well and 2 are greatly improved

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SYPHILIS

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SEROLOGIC TESTS

The Kahn Reaction

The quantitative Kahn reaction gives the titer of syphilitic serum in the same way that the Widal reaction gives the titer of typhoid serum, according to the inventor of the test, Dr. R L. Kahn.¹ He continues with the following claims for the quantitative Kahn reaction:

The quantitative titer of a syphilitic serum is obtained by making a series of

dilutions of the serum with salt solution and determining the highest dilution giving a positive precipitation reaction The titer is so computed as to correspond to plus signs. A titer of 4, 40 or 400 may be said to correspond to 4 plus, 40 plus or 400 plus. The titer of a serum depends on the concentration of syphilitic antibodies (or reagin) in the blood stream. The concentration of antibodies, in turn, is believed to depend on the degree of syphilitic activity in the patient, on his

capacity to produce antibodies, and upon other factors.

The quantitative reaction should be of value in the diagnosis of questionable cases when patients give no history nor clinical evidence of syphilis.

The quantitative reaction should prove of value also in the diagnosis if there is a history or clinical evidence of syphilis All indications are that low, moderate, and high titers correspond, in most instances, to low, moderate, and marked syphilitic activity.

The quantitative reaction should be employed in all conditions in which positive serologic reactions are obtained in the absence of syphilis. It would prove of great importance to establish the titers of positive reacting serums in leprosy, malaria, infectious mononucleosis, and other nonsyphilitic diseases. Indications are that the titers in these diseases are low, but no experimental evidence in this regard is available

The quantitative reaction is especially helpful in antisyphilitic therapy. A patient's serum giving a positive reaction might show a titer of 320 before treatment and perhaps titers of 280–160, 80, 20, 4, and finally a negative reaction after the patient has been given courses of therapy. Thus does the physician have a quantitative serologic record of his patient at any time during the entire period of therapy. The quantitative reaction may throw light on the efficacy of various methods of therapy.

The quantitative reaction may indicate the oncoming of a relapse in a syphilitic patient under treatment

The quantitative reaction is often helpful in serologically resistant cases. Records are available in which during 2 or more years of therapy of syphilitic patients, as many as 20 serologic reports were obtained, each marked "positive" or "4 plus". These 20 reports might have led to the assumption that the patients were "serologically fast." But the quantitative results in these cases revealed that at the initial serologic examinations, the patient's titers were relatively high, ranging from 200 to 800, while at the twentieth examinations the titers were close to zero, ranging from 2 to 4. The quantitative reaction frequently shows an immediate effect of therapy which is temporary and a later effect of therapy which is more permanent.

The quantitative reaction should help throw light on the interpretation of a therapeutic test. Thus, a patient may have a positive serologic reaction, but no other evidence of syphilis The quantitative test shows that the serum titer is, let us say, 4, 20, or 40 The patient is given a therapeutic test and quantitative determinations of the serum are made at frequent intervals, such as every other day Since, in most instances, therapy causes changes in the titer of a syphilitic patient, it would seem reasonable to assume that a therapeutic test followed by such changes has greater diagnostic value than a therapeutic test which causes no change in the titer.

Serologic Reactions for Syphilis in Blood Transfusions

Donors—In 1935, 15 cases of syphilis transmitted by means of blood transfusion were reported by Morgan who stated "that the occurrence of acute syphilis in recipients of blood is possible only when *Treponema pallidum* is present in the donor's blood and that this condition occurs only during the early stages of the infection and before the development of latency" Keller and Leathers² point out the incidence of serologic reactions which may be indicative or suspicious of a syphilitic infection in persons who offer to act as donors.

This investigation of serologic tests indicative of the prevalence of syphilis among 14,246 prospective transfusion donors shows that 1353 (95 per cent) of these tests were positive and that 252 (1.8 per cent) were doubtful. The incidence of 9.5 per cent in this group approximates closely the estimated incidence of 10 per cent of syphilis for the adult population in the United States. It is probable that a large proportion of the 1353 persons with positive tests indicative of syphilis did not know they had the infection All of the 1353 persons with positive tests were probably not informed that they had the disease this were done there was no follow-up procedure to confirm the diagnosis and to provide or advise adequate treatment

In view of this situation it is clear that some plan should be developed by hospitals that would lessen the rise of a hazardous outcome in individuals found to have positive serologic tests. It appears clear that if a hospital assumes responsibility for determining the suitability of individuals as transfusion donors, it also becomes responsible for informing these persons of the results of the serologic tests, particularly if the test is indicative of such an important infection as syphilis

Since July, 1937, a plan of notification has been followed in the Vanderbilt University Hospital whereby individuals who present themselves as blood donors are asked to specify whether or not they wish to be informed of the results of the serologic test in the event of a positive reaction. At the time the specimen is obtained they are requested to indicate on a special form whether or not they wish to be notified by letter.

During a period of 4 months (July to October), 825 donors were given serologic tests. Of this number, 679 were white persons of whom 18 (27 per cent)

were found to have positive reactions and 146 were negroes of whom 23 (15.7 per cent) showed positive reactions. In other words, 41 (5.0 per cent) of the total number examined were recorded as positive.

How to Check the Report of a Positive Serologic Reaction

No single test or single procedure uncontrolled or unchecked should be allowed to make a diagnosis of syphilis. In discussing this subject exhaustively, Stokes and Ingraham³ point out that the dependability of serologic results, and hence the quality of serologic test performance in syphilis, is critically important in all forms of legal regulations and they offer the following suggestions on how to go about checking the report of a positive serologic reaction.

The first inquiry should be into the source of the report and the methods used It is axiomatic, nowadays, that the report of a serologic reaction is worth only as much as the reliability of the laboratory from which it emanates and the responsibility and skill of the performer It is not to be expected that small private laboratories or even large State laboratories operating without interlaboratory check and without clinical control will be able to render the most trustworthy reports obtainable States in which a machinery for the serologic testing of applicants for marriage licenses or for pregnant women has been set up, or industrial organizations in which an attempt is made to provide an intramural laboratory service, should study and conform to the standards about to be set up by the United States Public Health Service

The time at which blood is drawn for the test and all attendant circumstances, including particularly the presence of intercurrent and especially febrile infec-

tions, must be taken into account in interpreting test results.

No single positive report should ever be accepted without confirmation. Repetition of the tests in the same laboratory by the same procedure is the least searching form of check. The performance of 2 or even 3 standard test procedures may provide additional interpretative evidence, but the difficulties of the interpretation increase with the number of tests and a corresponding degree of experience and expertness becomes desirable The sending of the blood to several laboratories is likely to increase the confusion and multiply the interpretative difficulties, though it is a proper check when conducted under sufficiently experienced direction Nonstandard or individual modifications of standard serologic tests for syphilis (for this country the Kolmer, Kahn, Kline, Hinton, Eagle procedures may be regarded as standard) are likely to lead to confusion and uninterpretable results This is especially true of the older multiple antigen and cholesterinized procedures.

Clinical examination in the doubtful case must be searching and conducted by one who is experienced in the recognition of individual, relatively unfamiliar signs, such as the Moon molar and other dental anomalies, the facies of prenatal syphilis, the less obvious evidences of early cardiovascular and neurosyphilitic involvement. It should be emphasized that the history of primary and secondary lesions taken as a routine has a margin of error ranging from 30 to 60 per cent or even higher and is practically worthless in women.

An examination of the spinal fluid should be conducted when, in the opinion of a reasonably expert reviewer of the evidence, it is actually necessary to do so Provocative procedure being open to suspicion, at least so far as the

arsphenamines are concerned, serial repetitions of the test will have to be substituted. The bismuth provocative procedure, even though resorted to in the foregoing cases, likewise has elements of uncertainty probably shared by all provocative procedures and is very much in need of reappraisal. Observation is, of course, a necessary element in any decision and absolutely essential if the weight of evidence pro and con approaches "50-50," so to speak.

A "no case" or negative decision inevitably involves some elements of subliminal or intuitive thinking. The necessity for a genuine acquaintance with the patient whose problem is under review, with his family, with all those who may have been drawn into the syphilitic infection from the standpoint of contact, family relationship and so on, may compel one to resort to epidemiologic case finding methods

The decision to treat on suspicion, while it seems an obvious resort, is nonetheless one for serious deliberation. Particularly is this so in women, for the problem of the infected woman is already uncertain enough from the standpoint of her ability to transmit the disease in a subsequent pregnancy, and the uncertainty can be multiplied many times by half-hearted or incomplete resort to treatment. The effects of treatment on serologic tests are unreliable as evidence in doubtful cases, so that the purpose of treatment is rather the protection of the individual and his contacts than the settlement of his diagnosis. It should be emphasized again and again that therapeutic tests on doubtful genital and secondary lesions can be interpreted only by experts and are of doubtful justification and validity at that. All in all, it is probably better, if the decision is made to treat, to ask the patient to go through with the full standard therapeutic regi-

men for the phase and stage of the disease in which he would be were the evidence of infection indubitable. Only in this way can he be given the best assurance that modern management of syphilis affords that he will be free of complications and fit for normal responsibilities.

DARK-FIELD EXAMINATION OF PUS FOR SPIROCHAETA PALLIDA

In the past there has been no method for converting a pus or blood contammated specimen into one suitable for adequate dark-field study. Friedman⁴ conceived the idea of centrifuging capillary tubes filled with pus at a low speed and thus obtain a cleared specimen of serum for dark-field examination

A number of fine straight glass capillary tubes about 12 cm. in length and of a constant bore was prepared Sections of glass tubing 6 mm in outside diameter and 13 cm. in length, sealed at 1 end, were prepared as receptacles for the fine glass capillaries. Undiluted gonorrheal urethral discharge was collected from dispensary patients of the Urologic Outpatient Department of the Hospital of the University of Pennsylvania. A number of the fine tubes were filled by capillarity with this discharge and 1 end of each tube was sealed by fusing in a small flame. The tubes were then placed in the receptacles and centrifuged in an international electric centrifuge, size 2, at various speeds and for various lengths of time. The lowest speed and the shortest time necessary to throw down all the cellular elements and leave a clear column of serum in the upper portion of the capillary tube proved to be 1000 revolutions per minute for 10 minutes. This speed was easily obtained with a small portable hand centrifuge, which was later substituted for the electric centrifuge.

A syphilitic rabbit testicle emulsion containing Spirochaeta pallida demonstrable by direct dark-field examination was mixed with gonorrheal urethral discharge so that the spirochetes could not be demonstrated by direct dark-field examination of the mixture. Capillary tubes were then filled with this mixture and centrifuged at 1000 revolutions per minute for 10 minutes. The tubes were filed and broken just above the line of separation of the sediment from the clear supernatant serum, which, after expulsion by pressure from a small rubber bulb, was subjected to direct dark-field study This examination readily revealed motile spirochetes.

This method for the dark-field examination of pus for *Spirochaeta pallida* was then tested clinically by applying it to a series of 40 patients with acute gonorrheal urethritis, all with typical purulent discharges. The capillary tube was applied directly to the pus appearing at the meatus of the penis and allowed to fill by capillarity. It was then sealed, centrifuged and cut as described, and the cleared serum examined for *Spirochaeta pallida*.

Friedman believes this method makes possible the dark-field examination for *Spirochaeta pallida* of small amounts of any body fluid, exudate or discharge capable of collection in a capillary tube

THE CONTROL OF SYPHILIS

The Rôle of the Physician—Syphilis constitutes one of the greatest of public health problems for 3 reasons: (1) Its great prevalence; (2) its ability to produce serious late lesions of the cardiovascular and nervous systems, and (3) the congenital transmission of the infec-

tion. Usilton estimates that there are over 500,000 new infections with syphilis in the United States each year, and it has been further estimated that if none of these infections was treated, about 25 per cent, or 125,000, would eventually develop serious cardiovascular or central nervous system involvement. Barnett⁵ points out that the importance of this disease as a public health problem is further enhanced by the fact that the means of its effective control are well known and he continued by pointing out the rôle that the physician plays in the desire to control syphilis

Modern treatment will not only prevent congenital transmission and the development of late lesions but it will also rapidly stop the transmissibility of the disease. The control of syphilis differs from that of any other infectious disease in that it depends only upon the proper application of antisyphilitic treatment, and isolation of any type during the infectious period is rarely necessary. The effectiveness of proper treatment cannot only be proved on theoretical grounds. but it has been demonstrated in Sweden⁴ where the incidence of new infections has been reduced from 6000 to 400 per year since 1919

The results were obtained in Sweden by making treatment compulsory in every case until the infection was entirely arrested. It is doubtful, however, whether legal control of this type would be effective in this country because of our much more mobile population. We have no laws for the control of venereal disease that resemble the Swedish ones, but other means of control are at hand that have never been properly utilized. Our complete failure to make progress in the eradication of syphilis during the last 20 years in which modern therapy has been in common use is largely due to the laxity of the medical profession in applying those measures that have always been available.

There is no excuse for the dismissal of a patient whose treatment has been inadequate. The principles of modern treatment have been clearly set forth in the publications of the Co-operative Clinical Group and have been fully abstracted in this review in the past few years.

When a patient lapses from treatment before it is completed, the fault usually lies with the physician and not with the patient. It is difficult to persuade a patient who has no symptoms and possibly even a negative blood Wassermann, that he needs prolonged treatment when this treatment is both expensive and uncom-Unless the reasons for the fortable necessity of such treatment are thoroughly explained, the co-operation of the majority of syphilitic patients will never be obtained The only time when a detailed explanation by the physician will be of the slightest value is before any treatment is given, and then it must be sufficiently convincing to offset any lay advice that may be subsequently received elsewhere

The first step in this instruction is to convince the patient of the accuracy of the diagnosis. The resistance to the acceptance of a diagnosis of syphilis is often great, and, unless a patient really believes that he has the infection, it is unlikely that he will submit to the necessary amount of treatment

After the physician is sure that the patient is willing to accept the diagnosis, he should outline in detail the probable course of treatment. Many patients become discouraged, and lapse from treatment after a few months because they are unable to get any estimate from the doctor as to the probable duration of therapy. The usual rapid disappearance of lesions and the early reversal of the Wassermann reaction should be pre-

dicted in cases of early syphilis, but it must be explained that in spite of this, treatment must be continued for a period of about 1½ years simply because previous observation has shown that relapse is altogether too common if less than this amount of treatment is given. The necessity of an examination of the spinal fluid at some time before the termination of treatment must be stressed. If the spinal fluid should prove to be abnormal, more than the estimated amount of treatment will probably have to be given.

Many patients in the later stages of the disease become discouraged and lapse from treatment because of apparent lack of progress. Usually this occurs because the Wassermann fails to reverse after months of treatment or because the Wassermann titer increases. The interpretation of the serologic tests is a difficult matter and the patient should be discouraged from attempting to interpret them himself He must be told that treatment 15 by no means guided solely on the basis of these tests and that they can often be entirely disregarded. The possibility of Wassermann fastness should be discussed Should this occur, special examinations of the cardiovascular and nervous systems including examination of the spinal fluid will be made. If involvement of either of these systems is found, proper treatment will be instituted to prevent serious damage. In case they are not found, the persistent positive reaction will be completely disregarded since clinical experience has shown that it does not indicate a serious prognosis, and treatment may be safely terminated in from 1½ to 2 years. It must also be stressed that the number of plusses in the serologic reports does not have the remotest relation to the severity of the disease and should be disregarded

The discovery of every person who has the infection is essential. The recent

educational program of the United States Public Health Service was instituted to acquaint the public with the widespread prevalence of syphilis and to teach something of the nature of the disease so that infected individuals will report to their physicians for treatment. This program will certainly fail unless physicians make a serious effort to trace all sources of recent infections and to examine for evidences of infection all contacts subsequent to the development of the disease.

Reactions to treatment are extremely unpleasant even when they are not serious, and they often lead to discontinuation of therapy They should consequently be regarded seriously and should always be treated with care

If proper care is taken by every physician who treats syphilis to insure the complete co-operation of his patients, to give careful and complete instruction before treatment is started, and to make a diligent search for sources of infection and infected contacts, great strides can be made in the control of syphilis whether or not improved laws for the control of venereal disease are passed.

The Teaching of Syphilis—The inability of the physician to cope with the problem of syphilis is sometimes traceable back to the teaching received in medical school. Moore, in discussing this problem, states that in many medical colleges the teaching of the management of syphilis is the same as in 1905.

The student comes into contact with syphilis in every department of the medical school. He encounters it first in pathology, where he learns the gross and microscopic alterations in the tissues which the infection may produce. In bacteriology, he learns something of the causative organism, the *Treponema pallidum*, and if he is fortunate in his instructor, he may have an opportunity to see the living germ by dark field together

with other spirochetes. Courses in immunology and serology are usually combined with those in bacteriology; and here the student sometimes learns too much technical detail of serologic tests before he possesses the fundamental knowledge which permits him to utilize them in interpretation.

When he enters the clinical field, he progresses through the major departments of medicine and surgery, in each of which he is faced with the differential diagnosis of the lesions of late syphilis. In obstetrics, he is taught the influence of syphilis on pregnancy. In pediatrics, he is instructed concerning the widespread range of manifestations of infantile and late congenital syphilis. In psychiatry, and relatively early in his clinical career, he begins to see the end results of syphilitic infection in brokendown paretics. In the several surgical specialties, he is confronted with a particular wealth of syphilitic material. In ophthalmology, he must learn something of the differential diagnosis of the commoner syphilitic eye lesions; and in neurology he is confronted with the intricate diagnostic problems of neurosyphilis.

The order of approach to the diagnosis of syphilis is such that the student obtains a distorted idea of syphilitic infection as an entity Usually, he learns something about early syphilis long after he is reasonably familiar with the late manifestations of the disease always he is led to believe that syphilis consists of a series of isolated manifestations which appear to have no clear connection with each other. Often the diagnostic information obtained from one clinical department is directly contradictory of that obtained from another. This dispersion of instruction, moreover, fails to provide any information concerning the epidemiologic and public health aspects of syphilis; and from the instructors in the various departments, the student obtains widely varying and wholly inadequate ideas as to treatment.

The centralization of such teaching in a single department is fortunately readily possible, since the professional care of syphilitic patients has already been so organized. The instruction given by this department should lay stress not, as in other courses in clinical medicine, on the differential diagnosis of syphilitic lesions, but, instead, on certain fundamental and comparatively elementary principles of diagnosis and treatment. In diagnosis, these principles are:

- 1 Syphilis is a prevalent disease.
- 2. Syphilis may often imitate or be imitated by other diseases.
- 3. Knowledge is essential, at least of the names, if not of the intricate details of differential diagnosis, of those diseases causing most diagnostic confusion
- 4 When confronted with any of these diagnostic possibilities, the student or physician should suspect syphilis
- 5 Modern laboratory tests are 95 per cent efficient in the diagnosis of untreated syphilis
- 6 Clinical suspicion must always be checked by these laboratory tests
- 7 The diagnosis of early syphilis is wholly a laboratory, not a clinical procedure

In public health the important principles are:

- 1. Syphilis is highly infectious during its acute phases
- 2 For every case of acute syphilis, there is a source of infection
- 3 This source spreads disease; it must be traced and rendered noninfectious, as must also all individuals whom the patient himself may have exposed
- 4. The arsphenamines and bismuth, in adequate amounts and by an appropriate system, control infectiousness.

In treatment, the important principles are:

1. The foundations for the serious late manifestations of syphilis are laid in the early stages of the infection.

- 2. The early stage is the important stage to treat, both from the individual and public health points of view.
- 3. Even after the golden opportunity of early treatment is past, congenital syphilis may be prevented; many of the late sequels can be forestalled; and symptomatic relief can often be obtained, even in apparently hopeless situations, by the adequate treatment of latent or chronic syphilis.

In addition, it must constantly be repeated that syphilis is a chronically relapsing disease, and the time relationships and the clinical characteristics of relapse and their relationship to infectiousness must be emphasized. Both in diagnosis and treatment, special stress must be laid on the 2 commonest late manifestations of the disease, cardiovascular and neurosyphilis. The student must know something of the economic aspects of treatment, of the fact that the proper management, even of the uncomplicated case, is a long drawn out, expensive procedure He must become expert in certain technical procedures in treatment, namely venipuncture, lumbar puncture, the technic of intramuscular injection. He must know something of the effect of drugs on the lesions of syphilis and, more particularly, on the patient himself. It does not suffice to cure syphilis and kill the patient. The mechanism of drug action, the toxic manifestations produced by the several drugs used in treatment, the choice of proper drugs for the individual patient, are all items with which he must become thoroughly familiar. He must learn that the treatment of early syphilis is a standardized procedure which should be carried out in every instance by a routine from which no deviation is permitted, except in the case of treatment reactions or complicating diseases He must know that the treatment of late syphilis is individualized rather than standardized, its intricacy often demanding wide clinical experience; and he must be aware of his own limitations in attempting the management of the late sequels. He must understand that often his best procedure is consultation with the expert when he encounters a situation with which he is not thoroughly familiar.

Other Considerations—At the present time, syphilis control centers about the finding of persons who may spread the infection to others because of open lesions from which spirochetes are transferred by contact, is the belief of Pearce.⁷

The destruction of these spirochetes is the first aim of treatment. Further, our methods for adequate prophylaxis are built upon the principle of such transmission. It is by no means certain, however, that our present ideas regarding the transmission of syphilis tell the whole story. It is theoretically possible that infection may be contracted from sources that are less evident than a visible lesion. A more complete knowledge of the disease might show that virulent spirochetes can be discharged from an apparently intact mucous membrane. If such should be the case, the question of the latent carrier and particularly the female latent carrier would take on a new and highly important significance. The effect on the epidemiologic aspects of the disease would be profound. We do not know as much about syphilis in women as we should That it differs in many important respects from the disease in men is well recognized but we understand very little of the reason for the differences.

To find and treat cases of syphilis adequately, the following public health services are needed, according to Parran:⁸ (1) A trained public health staff including a full-time medical officer to direct the control program, clinic physicians skilled in modern diagnosis and treatment of syphilis, public health nurses

to assist them, and field workers to find new cases and follow up lapsed ones; (2) reporting and follow-up of all cases of syphilis; (3) good treatment for patients with syphilis, including those who cannot pay, (4) access to free laboratory service for physicians and clinics making blood tests; (5) distribution of free antisyphilitic drugs to all physicians and clinics; (6) a required blood test for every expectant mother, (7) the requirement of medical certificates, including negative blood tests, before marriage; (8) the inclusion of blood tests in all complete physical examinations; (9) an adequate educational program aimed at age groups most frequently acquiring Public education is the crux syphilis of syphilis control. People must learn to consult doctors or clinics, and shun drug store remedies and self treatment as worthless The public must realize the cost of syphilis-in care, in wasted lives, in sorrow, and in dollars cheapest thing any community can do with syphilis is to cure it

THE PROGNOSIS OF SYPHILIS

The outlook for the patient with syphilis is dependent to a large extent on the management of the case by the physician in charge. Morgan⁹ brings together certain data concerning the disease in its natural, untreated state and assesses in the light of these data the value to the patient of modern treatment. He summarizes certain considerations which he feels the physician must keep in mind if he is to approach the therapeutic problem with confidence and optimism

It commonly occurs that syphilitic infection becomes established without manifestations of the acute stage of the disease. The recognition of its presence is then dependent on either serologic tests

or the ultimate evolution of serious sequelae. The incidence of cardiovascular syphilis and serious involvement of the central nervous system appear to be greater in patients who fail to react at the time infection occurs with acute lesions of the skin and mucous membrane than in those who experience these lesions. Thus asymptomatic infection seems particularly disposed to the ultimate development of serious sequelae. The frequency of asymptomatic infection in the female renders the general recognition of its presence and the prevention of congenital syphilis impossible without the employment of serologic tests of all pregnant women

The threat of untreated syphilitic infection to the individual is great. It constitutes a menace to personal contacts, the earlier the infection in terms of elapsed time from the initial lesion, the greater the menace. The pregnant woman with untreated syphilis has only 1 chance in 6 for a healthy living infant as compared with the normal woman's 3 chances in 4. There is some evidence that age, race and sex are factors in determining the morbidity and mortality of syphilis Syphilis in infants is commonly fatal In adult life, the negro male seems to be in a particularly vulnerable position with regard to cardiovascular syphilis and the white male with regard to neurosyphilis. The infection is less likely to result in serious disability in women, yet syphilis in pregnancy constitutes an extremely serious problem

With treatment, acute syphilis can be rendered noninfectious and "cured," and with the best treatment "cure" is possible in from 90 to 100 per cent of patients. From 70 to 80 per cent of patients with early latent syphilis can be "cured" in the practical sense of that word. The treatment of late syphilis is of the greatest importance, since it greatly reduces

subsequent morbidity and mortality from cardiovascular and benign tertiary syphilis. The early recognition and proper treatment of syphilis in pregnant women will greatly reduce prenatal and infant mortality and almost completely eradicate the tragic problem of congenital syphilis.

Criteria of Cure—If we are to suppose that the patient admitted with early syphilis has pursued the standard course of treatment for 1 year, as outlined, to be eligible for discharge he must have fulfilled the following requirements:

- 1. He must have completed 1 year (never less than 11 months) of regular and continuous treatment according to plan.
- 2 He must have been free from both external and serologic evidences of syphilis for not less than 6 months, and he must have received not less than 1 complete course of arsphenamine and 1 complete course of bismuth or mercury after the first negative Wassermann.
- 3 The spinal-fluid test (Wassermann, colloidal gold and cell count) must be negative at the end of the first year A negative spinal fluid at the end of the first course of treatment serves as an additional guarantee against neurosyphilis
- 4 A complete physical and neurologic examination, supplemented by roentgenograms of heart and aorta, and by electrocardiogram, must disclose no evidence of syphilis at the completion of the prescribed treatment

When a patient has completed the first year of standard treatment and has fulfilled the requirements for discharge, he should be told to return for a blood test at intervals of 3 months during the next year. If these trimestrial tests are consistently negative, he should return during the next 2 or 3 years at 6-month

intervals, and thereafter at yearly intervals.

A complete physical examination, including tests of blood and urine, should be given not less than once a year, and preferably every 6 months, after the patient has been discharged from treatment. Since the periodic physical examination is generally recommended, even for persons without a history of syphilis, it is obviously all the more important for those who do have such a history. The patient can easily arrange for a blood Wassermann to be added to the usual annual or semiannual physical examination, if this is not already a part of the routine procedure.

The physician who reads Cannon's statements about the inferiority of neoarsphenamine as compared with arsphenamine may feel that in neoarsphenamine he is seriously jeopardizing his patient's future The REVIEWER still believes in the efficacy of neoarsphenamine and is willing to reaffirm the statement made by the late Dr. Jay F. Schamberg some years ago that when neoarsphenamine "is rightly used the chances of success are almost equal to arsphenamine." The word "almost" is a partial admission of weakness, but as Dr Schamberg further pointed out, "the convenience of administration of neoarsphenamine and its lower toxicity are advantages that cannot be easily disposed of."

THE TREATMENT FOR SYPHILIS

Once the diagnosis of syphilis is established in a patient, it is advisable for the physician in charge to make out in advance for a year a scheme of treatment suited to the needs of the particular case. Cannon¹⁰ believes we are still far from having an ideal treatment plan, but out-

OUTLINE OF TREATMENT FOR EARLY SYPHILIS—THE PREFERRED ("3-2") PLAN

First 6 Arsphenamine Injections 3 Times a Week for the First Course First 6 Arsphenamine Injections 2 Times a Week for the Second and Subsequent Courses

	OLD ARSP	HENAMINE		MERCURY			SMU'		
Dose	Dosage for Men	Dosage for Women	Intervals BETWEEN Injections	Dosage* for Men and Women			age† en ai ome	nd	Dose
(104)	0 2 Gm.)	0 15 Gm	Mon	. ¾ gr. Hg	or	1	cc.		1st
o 2nd 3rd	0.2 Gm 0.25 Gm.	0 15 Gm. 0 2 Gm 0 2 Gm	Wed Fri Mon	¾ gr Hg	or	1	cc.		2nd
o 5th 6th	0 3 Gm 0.35 Gm 0 35 Gm	0 25 Gm 0 25 Gm	Wed Fri	¾ gr Hg	or	11/2	cc	Bı	3rd
7th {	0.4 Gm (03 Gm (Mon Fri	¾ gr Hg 1 gr. Hg	or		cc.		4th 5th
H 8th ∫ Sth	0.4 Gm ∫ 0.4 Gm	03 Gm ∫ 03 Gm	Wed	1 gr Hg	or	2 2 2	cc		6th
≝ 10th	0 4 Gm	03 Gm.	Tues	1 gr. Hg	or	2	cc		7th
Total	3 25 Gm.	2 40 Gm		1½ gr Hg	or	2	cc	Вı	8th
Four weeks' interval be- between 1st and 2nd			W eekly	1½ gr Hg	or	2	cc	Bı	9th
	arsphenamine courses		1½ gr Hg	or	2	cc.	Bı	10th	
Dose	0 2 Gm \ 0.25 Gm.	0.15 Gm }	Mon Thurs	1½ gr Hg	or	2	cc	$\mathbf{B}_{\mathbf{I}}$	11th
2nd 3rd 7	0.25 Gm.\ 0.3 Gm.\ 0.35 Gm.\	0 2 Gm (0 2 Gm (Mon Thurs	1½ gr Hg	or	2	cc	Bı	12th
5th 6th	0 4 Gm.	0 25 Gm 0 25 Gm	Mon Thurs	1½ gr Hg	or	2	cc	Bı	13th
a 7th	0.4 Gm	0 35 Gm	. Inuis	11 ₂ gr Hg	or			Bı	14th
z 8th o 9th	04 Gm 04 Gm.	0 35 Gm 0 35 Gm	Weekly	1½ gr Hg	or		cc	Bı	15th
∪ 10th ≌	04 Gm	0 35 Gm		Total Hg = 18 grains Total Bi = 27 cc = 1,350 mg					
				10tal Rt ~ 7					

Six weeks' interval between 2nd and 3rd arsphenamine courses.

(Cannon New York State J Med)

lines a plan of treatment worked out in the Department of Dermatology of the Vanderbilt Clinic.

Beginning Treatment — Without question the most gratifying rewards are to be had when treatment is begun within the first year of a syphilitic infection. The patient can quickly be rendered non-infectious—the most important consideration from the standpoint of public health; and since most patients with freshly acquired syphilis are young healthy adults, it is usually possible to carry out a regular plan of vigorous and thorough treatment, which provides the maximum chance for a cure with a minimum of risk. This early treatment is the surest preventive of the disabling forms of late

syphilis, involving the cardiovascular and nervous systems. When once these vital structures have been damaged, treatment must be largely palliative, and limited to checking further advances of the parasite

Continuous vs. Intermittent Treatment—Comparison of results achieved both in the Vanderbilt Clinic and elsewhere, under different systems of treatment, has amply demonstrated the superiority of continuous over intermittent treatment. The ideal is to keep the patient at all times under the influence of either arsphenamine or a heavy metal, and during the initial attack, in early syphilis, it is an additional advantage if both arsphenamine and the heavy metal courses can be given concurrently; there-

Third arsphenamine course Repeat dosage and intervals of 2nd course

Arsphenamine should total 30 injections (3 courses of 10 injections each) in the first year

As soon as 2nd arsphenamine course is completed, resume mercury or bismuth and give 2 more courses of 15 injections each at weekly intervals dosage as above Mercury or bismuth should total 45 injections (3 courses of 15 injections each) in the first year.

^{*}Dosage based on mercury salicylate \dagger Dosage based on preparations representing 50 mg of elemental bismuth in 1 cc

after they may alternate or overlap. When the patient is receiving only the heavy metal he should also be given potassium iodide by mouth. No "rest periods" should be prescribed in early syphilis; if the patient must miss treatment, as, for example, when traveling, he should take mixed treatment by mouth, or mercury rubs, or arrangements should

that neoarsphenamine may be successfully substituted for old arsphenamine in this scheme of treatment. The dosage must be one-third greater.

In the following outline of treatment for tertiary and latent syphilis, note that 2 months of mercury or bismuth medication precedes the use of an arsenical. This is extremely important in cases

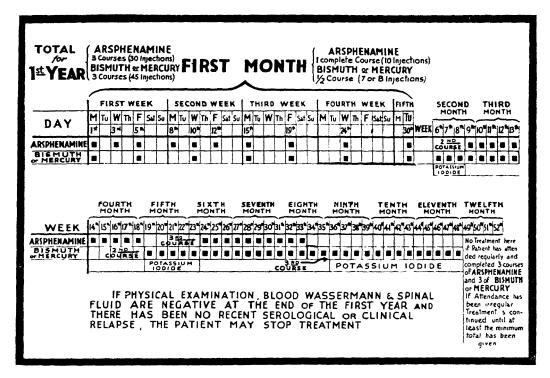


Fig 1-Outline of treatment for early syphilis (Cannon New York State J Med)

be made with a local physician or clinic to continue the treatment.

In the following scheme of treatment it will be noted that Cannon insists on the use of old arsphenamine which he states "will" bring about the healing of lesions and the reduction of a positive Wassermann to negative in a shorter time and with a smaller amount of the drug than did either neo- or silver arsphenamine in comparative studies. Because of the complicated technic of administering old arsphenamine and its greater toxicity the Reviewer believes

where there is danger of the "therapeutic paradox." For those who may not be familiar with this phrase, it refers to those cases in which intensive therapy benefits the syphilis but actually makes the patient worse. For example, to administer an arsenical to a patient with an enlarged syphilitic liver will rapidly reduce the size of the organ but this may cut off the portal circulation and result in a prolonged ascites whereas mild therapy gradually reduces the size of the liver and permits the establishment of a collateral circulation.

OUTLINE OF TREATMENT FOR TERTIARY AND LATENT SYPHILIS

Dose	OLD ARSPHENAMINE		Intervals	MERCURY	Візмитн	Dose
	Dosage Dosage for for Men Women		between Injections	Dosage* for Men and Women	Dosage† for Men and Women	
1st 2nd 3rd 4th 5th 7th 8th 9th	0.2 Gm. 0 2 Gm 0 25 Gm 0 25 Gm 0 3 Gm 0 35 Gm 0 35 Gm 0 35 Gm 0 35 Gm	0.15 Gm 0.15 Gm 0.2 Gm 0.2 Gm 0.25 Gm 0.3 Gm 0.3 Gm 0.3 Gm 0.3 Gm	All injections at weekly intervals Iodides 10-30 drops tid while patient is on mercury or bismuth alone	% gr. Hg % gr. Hg % gr. Hg % gr. Hg 1 gr. Hg 1 gr. Hg 1 ½ gr. Hg	or 1 cc B1 or 1 cc. B1 or 1½ cc Bi or 1½ cc Bi or 2 cc. B1 or 2 cc. B1 or 2 cc B1	1st 2nd 3rd 4th 5th 6th 7th 8th 9th 10th 11th 12th 13th 14th 15th

As soon as arsphenamine course is completed, resume mercury or bismuth, with iodides, and continue alternating courses of arsphenamine with mercury or bismuth for at least 1 year, with dosage and intervals as indicated above

* Dosage based on mercury salicylate † Dosage based on preparations representing 50 mg of elemental bismuth in 1 cc

(Cannon New York State J Med)

Simplified Technic for Administering Old Arsphenamine—For many years Cannon has maintained that old arsphenamine was the drug of choice in the treatment of early syphilis but admits there has been the following objections to its routine use "Old arsphenamme is usually given in very high dilutions, a procedure which necessitates the setting up of an elaborate gravity apparatus and the administration of large quantities of fluid Furthermore, it is very necessary that the acid arsphenamine solution be alkalınızed to exactly the right degree before it is injected or serious consequences may ensue" After studying these problems, consulting with the manufacturers of arsphenamine and long experimentation, the following simplification was evolved.11

Preparation of the Drug—The technic of preparing the concentrated solu-

tion for intravenous injection is as follows:

- 1 Pour sterile distilled water at room temperature into a sterile Erlenmeyer flask, to the amount of 5 to 10 cc for each decigram of the drug (Children tolerate easily down to 5 cc per decigram)
- 2 Immerse the ampule of arsphenamine in alcohol to detect cracks. Do not use any ampules which are cracked, or in which the powder is off-color (it should be pale yellow or lemon colored)
- 3. Dissolve the acid arsphenamine by sprinkling the powder on the surface of the water Avoid lumps, as they will not dissolve easily
- 4 Allow the solution to clear, be sure that there are no gelatinous masses.
- 5 Alkalinize the solution by adding the correct amount of sodium hydroxide from an ampule packed with the corresponding dose of arsphenamine
- 6 Rotate the flask gently, allow it to stand until the flocculate has cleared (The time required for this will usually be at least 15 minutes, but if the flask is covered and the solution remains at room temperature, it will

All tertiary cases should have, at the first visit, in addition to complete physical and neurological examination, tests of both blood and spinal fluid. No arsphenamine should be given to persons over 50 years of age unless stage of disease requires it and general physical condition permits it.

do no harm to let it stand even as long as 2 hours.)

7 Test for alkalinity with litmus; if red litmus turns blue, the solution is ready to be injected.

Equipment and Technic for Intravenous Injection—Twenty- to 23-gauge Fordyce needles with corrugated wing are used, with all-glass syringes. the syringe with a capacity of more than 20 cc., an adapter is necessary. needles must be sharpened smooth and both needle and syringe sterilized by boiling A fresh needle and syringe are used for each patient. Whereas the concentrated solution was formerly injected slowly and steadily, at the rate of 5 to 10 cc. per minute, lately better results have been obtained by using a method which for descriptive purposes may be designated as a stop-and-go method. It consists in injecting 3 to 5 cc of the solution at 1 time, pausing for from 20 to 30 seconds and then injecting another 3 to 5 cc, continuing with this alternation of injections and rest intervals until all of the fluid is injected. Under this method the patient suffers far fewer reactions than when the solution is injected steadily and continuously. In fact, confirmed nitritoid reactors are treated in this fashion without producing any ill effects. This favorable result is probably to be explained by the fact that the small amounts of arsphenamine solution given at each injection have time to become absorbed into the blood stream before the next dose enters, and thus the shocklike effect of the usual dose of arsphenamme on the organism is avoided

Intravenous Drip Therapy of Early Syphilis—Modern methods for rendering syphilis permanently noncommunicable require a minimum of from 8 to 10 months of treatment, and this time element is a serious obstacle to the eradication of the disease. In 1931 Hershfeld.

Hyman and Wanger reported a new technic "for introducing, with impunity, large amounts of fluids, drugs, and biologic substances by means of the intravenous drip" This method was applied by Chargin, Leifer and Hyman¹² for the administration of massive doses of arsenicals in the treatment of early syphilis. As recently reported by Hyman, Chargin, Rice and Leifer, ¹³ the technic is as follows.

The intravenous drips were set up so that 5 per cent dextrose was administered by the gravity method at a rate approximately 100 cc an hour. At the end of each hour there was added a solution of 01 Gm of neoarsphenamine dissolved in 50 cc. of 5 per cent dextrose In turn, this was followed by another 0.1 Gm of the drug until the total daily dose had been administered. Thus, in a period of 15 hours a patient might receive 1500 cc. of 5 per cent dextrose and 1 Gm. of neoarsphenamine. The treatment was usually started at 8 A M. and continued throughout the day, the needle remaining in situ The diet was semisolid and rich in carbohydrate.

In their most recent report in the Journal of the American Medical Association. Hyman, Chargin and Leifer claim that infectivity is of short duration with this treatment, spirochetes disappearing from lesions in 24 hours, and primary and secondary lesions healing rapidly.

Sobisminol Mass Given by Mouth—Several bismuth preparations designed for oral administration have been tried without conspicuous success. In 1937, Hanzlik, Lehman and Richardson introduced a product called sobisminol into the therapy of syphilis, a preparation which may be administered orally or intramuscularly Recently, Meininger and Barnett, ¹⁴ of the Stanford University School of Medicine, have claimed

that sobisminol mass is well tolerated when taken by mouth in therapeutically effective doses. According to these authors, "it produces rapid involution of lesions in early and benign late syphilis and causes the disappearance of spirochetes from the surface lesions of early syphilis. It appears to reduce the incidence of involvement of the nervous system but does not prevent a clinical or serologic relapse when substituted for intramuscular bismuth in the treatment of early syphilis. It is a valuable addition to antisyphilitic therapy and certainly deserves further clinical trial"

In the same Journal, Scholtz, Mc-Eachern and Wood¹⁵ make the following statements:

- 1 Sobisminol mass administered (daily) in doses containing about 0.84 Gm. of bismuth is absorbed from the gastrointestinal tract in a therapeutically active form in sufficient quantities to bring about involution of active syphilitic lesions of the skin. Involution is achieved in periods comparing favorably with those when preparations for intramuscular administration are used. The time required in cases of primary and secondary syphilis is only slightly greater than when neoarsphenamine is used.
- 2. Sobisminol mass (orally) in daily doses containing about 0.84 Gm of bismuth brings relief from the symptoms of late neurosyphilis (particularly tabetic) in a high percentage of cases and appears to offer a definite advantage over any drug heretofore used
- 3 Sobisminol mass (orally) is well tolerated by most patients. There is a high incidence of mild gastrointestinal reactions which rarely interfere with treatment. There are no reactions which compare in gravity to the embolism (arterial and venous) and abscess which occur with intramuscular injection with sufficient frequency to make them considerations for concern
- 4 Sobisminol mass can be administered every day for many months without producing cumulative toxic effects
- 5. Our material does not allow us to say that sobisminol mass (orally) can be substituted for other forms of bismuth in the routine treatment of early syphilis All circum-

stantial evidence points to the fact that sobisminol mass (orally) will do whatever any other bismuth preparation will do, but the ultimate proof lies in a treated series observed for several years.

- 6. Oral therapy has the disadvanatge that its efficiency depends on the intelligence and honesty of the patient (patients are frequently lax and dishonest to their own disadvantage).
- 7. If oral bismuth therapy receives approval, great care must be exercised in the control of its distribution. Self medication of syphilis is worse than no medication.

Based on the studies made on this drug, the Council on Pharmacy and Chemistry of the American Medical Association include sobisminol solution and sobisminol mass as new and nonofficial remedies with considerable comment.¹⁶

Choice of a Bismuth Preparation— In choosing the bismuth preparation to be employed, Cole and a group of his coworkers¹⁷ believe the physician should consider what is indicated in the particular patient

For rapid bismuth effect.

Sodium bismuth Injections intramuscutartrate in water Iarly 3 times a week

Sobisminol Injections twice weekly

If the patient can be persuaded to return twice a week for injections, probably the most efficient preparations in terms of high bismuth excretion are sobisminol and iodobismitol

For a somewhat slower but efficient bismuth effect:

Injections of oil suspensions of

Biliposol | Injections every 5 days to
Bismocymol | once a week

For an effect, slow in building up, but eventually sustained:

Sodium potassium bismuth tartrate

Bismuth subsalicylate.

Overtreatment in Syphilis—In the effort better to control syphilis in the United States, considerable emphasis has

been placed upon the necessity of adequate treatment from every patient with the disease. Cormia¹⁸ sounds a new note when he states that during the past few years he has observed several examples of a well defined overtreatment syndrome occurring in patients receiving continued neoarsphenamine and bismuth which, although well known to syphilologists has not received recognition in the literature.

This syndrome consists of symptoms referable to the nervous system as manifested by nervous irritability, insomnia, and headaches, to the gastrointestinal tract, as anorexia, chronic dyspepsia and constipation; to the respiratory system, as a chronic cough; and general weakness, malaise, and loss of weight. Cormia gives the details of 5 cases of overtreatment, 3 of which illustrate this syndrome, the fourth, lacking the syndrome, has manifestations of both bismuth and arsenical intolerance, and the fifth illustrates the influence of arsenical therapy in the production of some of the characteristic features

Because of continued positive Wassermann reactions, and against the advice of consultants to discontinue antisyphilitic treatment, the attending physicians continued their treatment of these patients although there was an increasing symptom-complex. In a comparatively short time after treatments were discontinued the symptoms disappeared in each case Three of the 5 patients had inactive, latent syphilis A fourth patient developed mucocutaneous relapse but was grossly overtreated with arsenic in relatively huge dosage, 09 Gm for a frail woman weighing 98 pounds. The fifth patient had central nervous system involvement of the paretic type which did not, of course, respond to standard antisyphilitic treatment.

Cormia feels that these cases exemplify the current medical trend of underexamination and overtreatment of the patient with syphilis. In latent syphilis particularly is the fetish of treatment carried to undesirable lengths, he says. Until the practicing physician makes a thorough initial investigation of every patient with a syphilitic infection before treatment is begun, until he asks himself what lies back of the positive Wassermann and makes a creditable attempt to differentiate late, inactive latency from active visceral syphilis, such tragedies will continue to occur.

Oral Treatment of Syphilis - In spite of the fact that oral treatment of syphilis has been repeatedly condemned, there are occasional attempts to revive it, particularly with new drugs The drug known as stovarsol, acetarsone or spirocid has called forth numerous conflicting reports, although such authorities as Moore, Stokes, Kemp and Poole have insisted that further chemical investigation is necessary before this drug can be accepted in the treatment of syphilis. Robinson and Robinson¹⁹ undertook the problem of further evaluating the drug as to spirocheticidal activity, contraindications, and advisability of its use as a routine therapeutic procedure discovered that Spirochaeta pallida could be demonstrated from surface lesions after the oral administration of 1 Gm of stovarsol or acetarsone a day for 3 days and it required at least 2 Gm. of this drug in 1 dose to cause disappearance of spirocheta pallida from surface lesions within 24 hours In only 4 of 25 patients with early syphilis did the serologic tests for syphilis become negative The number of reactions of the authors series was unusually high. Of 32 patients, 4 had dermatoses; 4 had diarrhea; 3 had an elevated icteric index; 1 patient had a severe gastrointestinal reaction with nau-

sea and vomiting and inability to retain the drug. In all, 37.5 per cent developed more or less severe reactions.

The authors concluded that the drug is a dangerous one and is contraindicated in the treatment of syphilis, especially as a self-medication.

Treatment-resistant Syphilis-The problem of treatment-resistant syphilis seems to be ever present and from the German and French literature one gains the impression that resistance to treatment is increasing Beerman reviewed the subject thoroughly in 1936 and grouped the numerous factors concerned as involving the host, the spirochete or the drug, either singly or through an interaction of 2 or more factors. The most commonly cited host factors are malnutrition, poor health, endocrine disturbances, hepatic insufficiency, failure of the cellular mechanism of the blood and faulty drug metabolism and intolerance to treatment. In a study of this problem, Beckh and Kulchar²⁰ found little evidence that specific host factors are primarily concerned in the production of treatment resistance. Likewise treatment refractories could not be ascribed to infection with a treatment resistant strain of Spirochaeta pallida

Treatment resistance was observed to occur with much greater frequency in patients treated by the "combined" (simultaneous, concurrent, continuous) system of therapy than in patients receiving the "alternating" type of treatment. It is suggested that the high incidence of treatment resistance observed among patients receiving the "combined" type of therapy is due to prolonged underdosage with the arsphenamines.

In the management of the treatmentrefractory patient, continuance of the same treatment is relatively ineffective. Intensification of treatment or change of drug or both is more frequently successful In patients refractory to these measures fever therapy is often effective.

Dangers of Arsenical Therapy in Syphilitic Pregnant Women—A critical analysis by Ingraham²¹ of the medical handling of the 42 cases of maternal death following antisyphilitic therapy during pregnancy reveals many interesting facts.

Statistics taken over a 5-year period in a large general hospital where the general principles involved in the teachings of the Co-operative Clinical Group on the management of syphilis in pregnancy are rigidly adhered to would indicate that under certain circumstances or with certain classes of patients during pregnancy there is a markedly greater incidence of treatment reactions than with other reported groups.

That this higher incidence of treatment reactions is not a peculiarity of the institution from which this series emanates is suggested by the 7 maternal deaths from antisyphilitic therapy reported from 6 different sources to the Committee on Maternal Welfare of the Philadelphia County Medical Society since 1931.

An analysis of the statistics pertaining to the 35 additional deaths collected from the literature indicates that the pregnant woman is not exempt from any of the severer types of treatment reaction, hemorrhagic encephalitis, acute circulatory collapse, damage to the liver, arsphenamine dermatitis, and aplastic anemia, all having occurred with fatal termination. There is, moreover, evidence to indicate that antisyphilitic therapy may aggravate an already existing toxemia or precipitate an incipient one.

This presentation is not intended in any way to depreciate the value of ante-partum antisyphilitic therapy in protecting the unborn child in utero. All the authoritative literature indicates that at present the treatment of infected preg-

nant women forms one of the best imaginable fields of preventive medicine.

The added impetus of the public health movement for control of venereal disease, and especially the attention directed toward syphilis in pregnancy by the numerous state antepartum and premarital Wassermann laws under discussion, will tend, of necessity, for a time at least, to direct the treatment of many syphilitic pregnant women away from the medical specialists in this field. While it is undoubtedly true that, with a rare degree of intuitiveness, individualization and attention to detail such as may be expected from the expert, it is possible safely to treat syphilitic pregnant women with arsenicals, the facts contained in this study would seem to suggest that it is hardly proper to state that these women tolerate such therapy as well as or better than average.

The fact that these unfortunate symptoms have tended to occur among young patients with early or symptomless syphilis indicates that even with such patients, who if not pregnant would be expected to tolerate active therapy well, it is advisable to administer arsenical treatment cautiously, starting with small doses and gradually increasing them Moreover, since for the pregnant woman the drug is ordinarily not curative but prophylactic for her child, it would possibly be advisable to give more consideration to adequate preparatory heavy metal therapy before commencing active arsenical treatment, even though one is confronted with an early infection in late pregnancy.

In addition, the question is raised as to whether active arsenical therapy is indicated at all during pregnancy unless there is reasonable assurance that the prospective infant has a strong chance of being diseased

Moore²² discusses Ingraham's paper in an editorial, and states that the choice

of material has led Ingraham into an important statistical error which materially affects the validity of his conclusions, and questions the validity of a number of his statements. The subject is an interesting and important one and worthy of further research.

Hepatic Reactions to Treatment for Syphilis (Jaundice)—Lane²³ presents a detailed discussion of the various factors which may be involved in the development of jaundice in 100 patients with syphilis under antisyphilitic treatment. In his summary and conclusions, he says.

"One hundred cases of jaundice occurring in the course of antisyphilitic treatment have been reviewed

"Syphilis alone seems a relatively rare causative factor.

"Arsenic alone, except in cases of sensitivity to arsenic or of variance in the hepatotoxicity of the preparation, does not account for the disease in many cases. One cannot escape the impression, however, that it has some effect in the majority of cases

"Bismuth, with treatment in 60 per cent of cases in this series interrupted by jaundice during the course of bismuth medication, appears to participate to a greater degree than is usually accepted

"Three cases of 2 attacks of jaundice are reported

"Eleven cases in which jaundice occurred during tryparsamide treatment are mentioned

"Three deaths occurred, 2 from cirrhosis

"Bismuth and arsenical therapy in conjunction with some mild infection can exaggerate the damage inflicted by *Spirochaeta pallida* on hepatic cells and produce jaundice as a complication of therapy"

In keeping with Lane's properly conservative conclusions regarding his experience, the complete lack of understanding of the etiology and pathogenesis of so-called postarsphenamine jaundice is well brought out in the discussion which followed the presentation of the paper before the sixty-first annual meeting of the American Dermatological Association.

O'Leary said: "I believe that a discussion of postarsphenamine jaundice would be incomplete if one failed to mention the fact that jaundice which appears in a patient who has received treatment for syphilis may be in no way related to the syphilis or to the treatment. Extrahepatic factors . . . must be borne in mind, as well as arsenic, syphilis or some other infectious agent, as the cause of the icterus."

In discussing the treatment of postarsphenamine jaundice, Soffer²⁴ offered the following conclusions:

- 1 When the clinical and experimental data presented in the literature concerning the treatment of arsphenamine jaundice are analyzed, one is impressed with the fact that a high carbohydrate diet is well accepted as an important therapeutic measure (Stokes states that a diet "high in proteins and fats and low in carbohydrates" is valuable, not in the hepatic accidents as such, but in the prevention of cutaneous irritability. In hepatic accidents he favors a high carbohydrate diet.)
- 2. Such diets should consist of 400 to 600 Gm of carbohydrates per day divided into 5 or 6 feedings
- 3 Those carbohydrate foods should be employed which are made up essentially of fructose and glucose, since these sugars are most readily converted into glycogen by the liver Thus, cane sugar, which is hydrolyzed into glucose, honey, which is mostly glucose and fructose, and fruit junces are most desirable
- 4 Where the amount of carbohydrate taken orally is madequate, diets should be supplemented by a constant intravenous drip of 5 per cent glucose
- 5 Insulm should be employed only when glycosuria is manifested
- 6 The use of cholagogues and choleretics in the treatment of arsphenamine jaundice is an unsound form of therapy.

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THERAPEUTICS

By Henry F. Page, A.B., M.D., and Malcolm W. Miller, A.B., M.D.

ACETARSONE

Effective therapy, for any disease, depends on numerous factors, the most important of which are: (1) Efficiency of the therapeutic agent; (2) ease of administration; (3) co-operation of the patient, or the patient's family, with the physician; (4) a low degree of toxicity

In the search for satisfactory drugs to combat syphilis, acetarsone has recently shared the spotlight. This preparation, given by mouth, has been used rather extensively in the treatment of congenital syphilis

Pillsbury and Perlman¹ have recently published an excellent review of acetarsone therapy, in which they indicate that the preparation possesses undoubted value, is not without danger, and warrants further extensive investigation

Optimum dosage has not definitely been established, but the above investigators indicate that doses, somewhat below the usually recommended levels, are preferable

Although the action of acetarsone is less rapid than that of arsphenamine, it is, nevertheless, an active antisyphilitic agent when given by mouth. For patients under 6 months its effect, in reversing the Wassermann and Kahn reaction of the blood, has been only moderately satisfactory. For patients over this age, it has been as good as standard preparations.

The incidence of all reactions in Pillsbury's series has been 107 per cent, that of serious reactions, particularly nephritis, 46 per cent. Nephritic reactions, occurring suddenly and insidiously, are the greatest single drawback to acetarsone therapy. The administration of the drug should not be resumed after such a

reaction. In general, the occurrence of gastrointestinal and dermatitic reactions does not contraindicate further acetarsone therapy.

Acetarsone is probably not administered as directed to patients treated at home. The incidence of reactions among patients treated under controlled conditions in the hospital is reported by Pillsbury and Perlman to be 4 times that observed among outpatients. Regularity of attendance apparently is not increased by oral therapy as compared to injection.

The effect of acetarsone in arresting congenital syphilis is inferior to that of arsphenamine and bismuth preparations. The incidence of reactions is high; acetarsone cannot be controlled by experimental studies of spirocheticidal action and toxicity in animals, and administration to outpatients is not assured.

ADENINE SULFATE

The successful use of adenine sulfate in granulocytopenia following surgical sepsis was reported by Richmond ² The material was prepared by dissolving the salt in normal saline, 15 grains to 3½ ounces (1 Gm. to 100 cc) boiling, and giving intravenously. Two Gm were given the first day with immediate response, which continued after repetition of the dose the next day. Previously, the patient had not responded to liver or pentonucleotide.

ADRENALIN (EPINEPHRINE)

Since the isolation of epinephrine by Abel, investigators have attempted to produce more active compounds with more prolonged effectiveness

During recent months 2 preparations have come into being, which represent great strides in adrenalin therapy, particularly in respect to their use in allergic conditions, such as asthma.

The first of these preparations was reported by Keeney, Pierce and Gay³ and is a suspension of powdered epinephrine base in peanut oil, prepared so that 15 minims (1 cc.) of oil contains $\frac{1}{30}$ grain (2 mg.) of epinephrine.

The rationale of using this preparation was predicated on the observation that oils, when given parenterally, are slowly absorbed, and that this circumstance would permit the use of such a preparation in doses of 2 to $2\frac{1}{2}$ times the strength of the usual 1:1000 saline solution of epinephrine ⁴ Its effect differs from ordinary solutions of adrenalin only in that it lasts over a longer period of time, reputedly 9 to 16 hours

The dosage may be from 7½ to 22 minims (05 to 15 cc) with an average of 15 minims (1 cc). It is given either intramuscularly or subcutaneously, being somewhat less irritating by the intramuscular route. The administration of the oil preparation requires a dry sterilized syringe and needle, the latter of large bore. The solution may be sufficiently liquefied by holding the vial in the hand for several minutes. Untoward reactions are those of ordinary adrenalin solutions.

The second slowly absorbed adrenalm preparation is "gelatin-epinephrine mixture" and was reported by Spain, Strauss and Fuchs ⁵

This mixture, like adrenalm in oil, is a 1 to 500 preparation and possesses the same important attribute of being slowly absorbed. Roughly speaking, its action lasts from 8 to 12 or more hours. It is described as being nontoxic, nonantigenic, and readily administered by the patient. This last feature is the chief advantage claimed over the oil preparation, in that

it can be easily administered with the ordinary syringe and needle. The mixture is a gel at room temperature, and at the lower temperature of the refrigerator (41° F.—5° C) in which it should be stored. For administration, it must be liquefied by warming. This is most easily accomplished by placing the vial in a container and covering it for a few minutes by hot water. The syringe is used while warm, and need not be dry.

When either of these preparations is used in allergic individuals in place of the aqueous solution, a sharp reduction in the daily number of required doses of epinephrine is noted. A marked clinical improvement frequently results.

AMINOPHYLLINE

The use of aninophylline as a diuretic and possible coronary dilator and myocardial stimulant has long been accepted, but Brown⁶ calls attention to its use to relieve bronchial obstruction in asthma. He uses 4 grains (0.24 Gm.) in 2½ drams (10 cc.) of distilled water, normal saline, or dextrose. The mode of action as yet remains unexplained.

AMINOPYRINE

This antipyretic and analgesic drug continues to be investigated as the primary causative factor in many cases of malignant neutropema

Butt, Hoffman and Soll⁷ have shown experimentally in dogs that animopyrine has a selective toxic action on bone marrow. The end result is one of severe aplasia of the bone marrow, rather than of hyperplasia with "maturation arrest"

These authors further conclude that ammopyrine is only one of a variety of agents causing malignant neutropenia, although an important one.

Certainly the promiscuous use of this drug is to be condemned, and it should be prescribed with extreme caution and close observation, if prescribed at all.

AMPHETAMINE SULFATE (BENZEDRINE SULFATE)

The scope of this drug's therapeutic usefulness is steadily widening. Its dangers have been reported as minimal and its margin of safety very wide

During the past year a note of caution has been dropped into the medical literature, indicating that an overindulgence in the drug, by a sensitive, fatigued individual may have disastrous results, even death.

L. C Smith⁸ reports a case of a male university student, aged 25, who, while writing an examination, began suddenly, to snore loudly, made "funny noises" and in a few minutes ceased to breathe.

Autopsy revealed a congested, tense, liver, a dilated stomach, some congestion of gastric mucosa, but otherwise normal findings. Stomach contents, which were large in quantity, contained traces of amphetamine. The student's roommate contributed the information that the patient had been making a practice of taking 1 /₁₂ grain (5 mg) of the drug half an hour before each examination. During the 4 days prior to his death, he had had about 6 examinations. A 25-tablet bottle among the patient's possessions contained only 10 tablets.

Four factors figure prominently in the student's death. They are a large meal, the nervous tension of the examination, fatigue, and amphetamine sulfate. Probably no one of these factors would have caused a sudden collapse with death in a healthy person, such as the patient was It is known that severe collapse can occur following the use of amphetamine

sulfate in fatigue state, so that, although not definite, it is probable that the drug contributed to the fatal collapse in this case.

The primary conclusion to be drawn from the above report is that the promiscuous use and drug store sale, without a prescription, of amphetamine sulfate, as a "pep pill," should be discouraged.

Good results continue to be reported in the use of amphetamine in chronic alcoholism 9, 10. It is suggested that the use of this drug may permit a sufficient interval of sobriety for the institution of the usual and more fundamental psychotherapeutic methods. This interval is, perhaps, made possible by substituting the "lift" of amphetamine for the "lift" derived by the chronic alcoholic from his chosen nectar. The dose of amphetamine in these cases varies, according to the individual's susceptibility and requirements, but, in general, 15 ½ grain (10 mg.) twice daily.

There has been some indication that another valuable use of this drug may well prove to be in the treatment of drug addictions, including both the barbiturates and the morphine derivatives, and studies of its value in these cases are awaited with interest.

ANTIPNEUMOCOCCUS SERUM

Although in the past year emphasis has definitely been on chemotherapy for pneumonia, nevertheless serum therapy still remains the one definitely established method of treatment with a definitely known improvement in mortality. Many favorable series of cases, covering several years of study, continue to be reported with the use of antipneumococcus serum

Bullowa¹¹ summarizes the advantages and disadvantages of serotherapy "Antibody neu-

tralizes capsullar substance which either is already present in the body or develops during several days when sufficient serum is given.

"Pneumococci are not dissolved or phagocyted unless they are sensitized by antibody. This may be autogenous or injected when vicariously produced in horses or rabbits

"Pneumococci have their virulence reduced when grown in the presence of antibody."

The disadvantages are as follows:

"Serum administered must be specific for the infecting type.

"Some types, especially those which produce a very large amount of antibody, such as pneumococcus Type III, are resistant to serum

"Serum must be given intravenously and requires devotion on the part of the physician

"Though unfavorable reactions may be forestalled, there is always the possibility of anaphylaxis, thermal reactions and serum sickness

"Serum therapy is expensive"

Horn¹² summarizes 245 cases of lobar pneumonia with a mortality of 3.6 per cent—Type I. In all his serum-treated cases, the death rate is 3.3 per cent Serum sickness was observed in only 12 cases.

Finland and Brown¹³ in 459 cases of Type I had a mortality of 19 per cent and in 385 controls a mortality of 40 per cent. They came to the conclusion that Type I antipheumococcus serums produced in both horses and rabbits were potent and effective and that there was insufficient data to indicate any superiority of the 1 over the other.

In a similar study of Type II, Type V, and Type VII pneumonias, these same authors¹⁴ found in 141 serumtreated cases of Type II pneumococcus pneumonia a mortality of 19 per cent. The death rate among 64 contemporaneous nontreated serum cases was 64 per cent. The untoward reactions to serum injections were more frequent in Type II cases than in Type I cases. Concentrated rabbit serums were used in the treatment of patients, including 4 with bacteremia.

None of these patients died. They therefore concluded that the high potency of these Type II rabbit serums may prove to be preferable to horse serums in the treatment of pneumococcus Type II. In 81 cases of Type V, and 9 cases of Type VII pneumococcus pneumonia, they had equally favorable results

Volini and Levitt¹⁵ used concentrated rabbit serum in 153 cases of all types. They found the mortality was 4 times less than in the nonserum-treated cases. They noted that sensitivity to the therapeutic rabbit serum is rarely encountered, being remarkably free from immediate reactions and producing a relatively small percentage of thermal and delayed serum reactions. It lent itself to the concentrated single dose administration which saves much time and probably enhances its therapeutic efficiency

Barry Wood¹⁶ ran a series of 50 patients treated with concentrated rabbit serum. Eight patients with Type 3 pneumonia died, the serum seeming to be relatively ineffective in this type. For the remaining 42 patients, the fatality rate was 143 per cent, although 26 per cent of the patients had bacteremia and a like number had multilobar consolidation.

Edwards, Hoagland and Thompson¹⁷ introduced an intracutaneous test with type specific pneumococcic polysaccharide as a guide in serum therapy. In 114 cases of lobar pneumonia caused by Types 1, 2, 5, 7, 8, or 14, type specific antipneumococcus rabbit serum was used The reaction of the patient to intracutaneous tests with the type of specific polysaccharide from the capsule of a homologous type of pneumococcus was determined before, during, and after the administration of the serum. In 110 of the patients there was a negative reaction to the test, indicating a low content of circulating antibody before serum was

given. The test proved to be a valuable aid in the more accurate estimation and control of the optimum dose of serum necessary for the successful treatment of the patient. In 35 cases, daily skin tests with the polysaccharide were performed until the patient was discharged from the hospital. In 12 of these cases, the reaction became negative before the patients were discharged and in 23 it remained positive. In some cases without complications a positive reaction to the skin test at the time of admission on the sixth and seventh days of the pneumonia enabled them to withhold treatment, with the assurance of the presence of sufficient antibodies to cause a crisis with favor-They conclude that the able outcome polysaccharide is a valuable although not infallible means for measuring the serum required for treatment in a given case of pneumococcic pneumonia.

ATROPINE METHYLNITRATE (EUMYDRINE)

Dobbs¹⁸ reports a series of 20 infants with pyloric stenosis treated with atropine methylnitrate (eumydrine). Sixteen of these were cured, 3 were operated on successfully after eumydrine had failed to relieve the vomiting, and 1 died during treatment. Diagnosis was made on a typical history—visible peristalsis and a palpable pyloric tumor. Dehydration and alkalosis were relieved by the subcutaneous injection of normal saline before eumydrine was administered and were continued as long as daily fluid intake was insufficient Gradually increasing doses of 1 to 10,000 solution of eumydrine were given 20 minutes before each feeding, beginning with 15 minims (1 cc.) and reaching 1 to $1\frac{1}{2}$ drams (4 to 6 cc.) each feeding Gradually increasing amounts of either breast or bottle milk were given after an initial starvation of 12 to 18 hours, and an initial, and thereafter daily, stomach washout was given until the residue became negligible. Infants were discharged as soon as vomiting was controlled and treatment was thereafter continued in the home. Eumydrine was discontinued after gradual diminution of the dose from 12 to 16 weeks, depending on response to the drug. Transient flushing in 1 case receiving 8 cc. of eumydrine per dose was the only observed symptom of atropine-like poisoning.

BISMUTH

The treatment of syphilis would undoubtedly be facilitated by the discovery of a bismuth preparation which is effective when taken by mouth.

Recently, work has been reported on the use of sobisminol mass. This substance is given in capsules, each containing 3 grains (0.2 Gm) of sodium bismuthate, 6 grains (0.4 Gm) of trusopropanolamine and 1½ grains (0.1 Gm) each of propylene glycol and ethyl alcohol. The bismuth content of each capsule is $2\frac{1}{3}$ grains (0.15 Gm).

The prescribed dosage averages 1 to 2 capsules 3 times daily Larger doses are sometimes given, but Meininger and Barnett¹⁹ report 2 capsules 3 times daily as the apparent optimal dose.

These authors report that "sobisminol mass is well tolerated when taken by mouth in therapeutically effective doses. It produces rapid involution of lesions in early and benign late syphilis and causes the disappearance of spirochetes from the surface lesions of early syphilis. It appears to reduce the incidence of involvement of the nervous system but does not prevent a clinical or serologic relapse when substituted for intramuscu-

lar bismuth in the treatment of early syphilis. It is a valuable addition to antisyphilitic therapy and certainly deserves further clinical trial."

Toxic reactions are apparently not frequent or marked. They include: Bismuth line; stomatitis, nausea and vomiting, anorexia, diarrhea, urinary frequency, ptyalism and parotitis, and esophageal spasm.

Scholtz, McEachern and Wood²⁰ confirm the studies of Meininger and Barnett¹⁹ and further conclude that "our material does not allow us to say that sobisminol mass (orally) can be substituted for other forms of bismuth in the routine treatment of early syphilis. All circumstantial evidence points to the fact that sobisminol mass (orally) will do whatever any other bismuth preparation will do, but the ultimate proof lies in a treated series observed for several years."

Oral therapy has the disadvantage that its efficiency depends on the intelligence and honesty of the patient (patients are frequently lax and dishonest to their own disadvantage)

If oral bismuth therapy receives approval, great care must be exercised in the control of its distribution. "Self-medication of syphilis is worse than no medication."

BLOOD BANK

In the past year, the blood bank idea has been received more and more enthusiastically both at home and abroad, but, as yet, no final decision has been reached as to its final status. Kolmer²¹ points out certain differences, such as:

(1) While sodium citrate is slightly anticomplementary, the complement of citrated human blood kept at 39 to 43° F (4 to 6° C) was well preserved for periods up to 14 to 16 days

- (2) The bactericidal activity of normal citrated blood kept at 39 to 43° F. (4 to 6° C) for S. aureus, Beta hemolytic streptococcus, and B coli decreased after 7 to 21 days preservation.
- (3) The phagocytic activity of the neutrophils of preserved citrated human blood was definitely reduced within 72 hours after collection of blood, becoming markedly so, on, or about, the fifth day.
- (4) The erythrocytes of preserved citrated human blood kept at 39 to 43° C (4 to 6° C) showed evidences of swelling and dehemoglobinization as early as 48 hours after collection, with progressive degenerative changes up to 14 days, when at least 30 per cent were shadows, swollen and fragile.
- (5) The neutrophils of preserved citrated human blood kept at 39 to 43° F. (4 to 6° C) showed evidences of disintegration with reduction in numbers as early as 24 hours after collection.
- (6) The platelets showed distinct clumping immediately, and 24 hours after collection, with evidences of deterioration in the latter. At the end of 48 hours, they became scarce and after 5 days, only blue chromatin masses remained

Therefore, the author believes that citrated human blood preserved at 39° to 43° F (4° to 6° C) may be useful in the treatment of acute hemorrhage and shock, for the purpose of restoration of volume, but is inadvisable for the treatment of anemias, blood dyscrasias, or infections

Belk, Henry and Rosenstein²² noted similar changes, that is, an increase in the fragility of the red cells, disintegration of the granulocytes, and impairment of the properties of coagulation, all progressive. In 400 consecutive transfusions with stored blood, jaundice, or hemoglobinuma, although of a harmless character were observed 7 times.

CALCIUM (AS A SYNERGIST WITH DIGITALIS)

The use of calcium salts in conjunction with digitalis has long been con-

demned because of reputed increase in toxicity of each, due to a synergistic action of the 2 drugs.

Smith, Winkler and Hoff²³ have indicated, as a result of careful animal experimentation, that the lethal effects of calcium and digitalis are neither synergistic nor even completely additive.

It is further probable that the findings of potentiation reported in the literature are due to 2 factors: (1) Sudden death from ventricular fibrillation produced by calcium at unusually low levels, which occasionally occurs in normal animals; and (2) the fact that half the acute fatal dose of digitalis may kill, within an hour or more, approximately half the animals to which it is given.

A lack of additive effect or of potentiation does not, however, mean the administration of calcium chloride to digitalized patients or to any patient is an entirely safe procedure. Calcium chloride alone, given intravenously to normal animals, is a toxic drug. Its administration to a patient whose failing circulatory system has already occasioned the use of digitalis is probably more dangerous than its administration to other patients, since calcium, like digitalis, has been shown to produce death by circulatory failure.

Smith, Winkler and Hoff²³ suggest that the danger of injecting calcium into the digitalized patient is simply that of injecting calcium into any patient with cardiac disease, and that this, in turn, probably involves only some intensification of the danger involved in injecting calcium intravenously into a healthy subject. Their experiments further indicate that whatever danger is involved in the intravenous use of calcium can be minimized by very slow injection of the salts, so that the local concentration in the heart never attains an unsafe level.

CARBON TETRACHLORIDE

Smetana²⁴ reports 3 cases of carbon tetrachloride poisoning. In addition to hepatic damage, he demonstrated that carbon tetrachloride causes alarming renal symptoms, such as oliguria or anuria, nitrogen retention, and subsequent hypertension The urine may contain albumin, white blood cells, red blood cells, casts and bile. The anatomic basis for the clinical renal symptoms is nephrosis, characterized by distention of the spaces of Bowman with albuminous precipitate with swelling of the lining cells, swelling and vacuolation of the cells of the proximal convoluted tubules, degeneration, and necrosis of the cells of the distal convoluted tubules and those of the loop of Henle, with desquamation, and by the presence of granular hyalin and cellular casts in the tubules with plugging of their lumens.

CEVITAMIC ACID

The chief contribution to therapy with cevitamic acid, during the past year, has been the demonstration that intramuscular injection of the monoethanolamine salt of this acid is extremely efficacious in patients exhibiting vitamin C deficiency ²⁵

In certain patients who cannot tolerate cevitanic acid by mouth, or in whom gastric anacidity or the presence of pathologic changes in the bowel leads to destruction or poor absorption of the vitamin, the parenteral administration of vitamin C is an established clinical necessity

It has been shown that the intramuscular injection of the monoethanolamine salt of cevitamic acid, in average daily doses of 1½ grains (100 mg.), is effective in patients with marked vitamin C deprivation, and causes no immediate, or delayed, local or systemic reaction.

CHAULMOOGRA OIL

Stanley²⁶ reports 50 ambulatory cases of atrophic, hypertrophic, and mixed arthritis treated with intramuscular chaulmoogra oil. Graduated doses of from 15 to 75 minims (1 to 5 cc.) of the crude chaulmoogra oil mixture were given. Often no relief was experienced until after as many as 25 injections, but a definite response was obtained in some cases after 3 injections. Continuity of treatment is imperative. The most satisfactory results were obtained with acute and subacute types of arthritis. In the presence of complete ankylosis, the prognosis is distinctly unfavorable No exact statistical or clinical evaluation. however, is presented.

COBRA VENOM

Because the care of the patient with advanced cancer, or other incurable painful states, is such a perplexing problem, particularly for patients who cannot afford institutional care, or for whom opportunities to obtain it are lacking, the use of cobra venom has been suggested as a more ideal treatment than the administration of opiates every 3 or 4 hours.

The use of this substance has been described by Rutherford 27

It is said that after saturation is obtained, the action of venom lasts 2, 3, and sometimes 4 days. Apparently the action of cobra venom is one of central analgesia, and may be likened to the action of digitalis, in that the patient undergoes a period of saturation for 3 to 6 days. During this period of time, the patient is given intramuscularly an initial daily dose of 7½ minims (0.5 cc.) or 2 mouse units, and subsequent daily doses of 15 minims (1.0 cc.), or 5 mouse

units, until saturation is reached, as determined by clinical relief of pain. After this, the maintenance dose is dictated by the physiological needs of the patient; that is, the amount and character of the pain Occasionally some supplementary, quick action, analgesics are necessary.

To date, there has been no evidence of addiction or of increased tolerance to this substance, and, in the dosage advised, no undue toxicity.

COLLOIDAL ALUMINUM HYDROXIDE

A gastric antacid is a chemical substance introduced into the stomach for the purpose of lowering the hydrogen ion concentration, or acidity, of the gastric contents. Such antacids are in common use in medical practice, mostly in the treatment of peptic ulcer. Unexpected difficulties are often encountered in the use of antacids to lower gastric acidity, because no antacid has yet been found which will simply neutralize acid without exhibiting additional pharmacologic action ²⁸

On the basis of its merits and freedom from the undesirable qualities of most antacids, it seems justified to state that colloidal aluminum hydroxide is the most satisfactory antacid thus far employed Constipation, which is usually easily controlled, is the only objection to the use of this substance which has thus far been mentioned.

Colloidal aluminum hydroxide is a white, gelatinous substance, mildly astringent and nonirritating. It is amphoteric, with a pH of 6.9; hence it may be administered continuously without danger of alkalosis. The preparation contains about 5 per cent aluminum hydroxide and 06 per cent sodium chloride; the remainder is water.

Methods of administration vary.²⁹ The substance may be diluted to 25 per cent and continuously instilled into the stomach through a nasogastric tube at the rate of 15 drops per minute, both day and night, for 10 days, after which it is administered orally.

It is perhaps more frequently given by the oral route in doses of about 1 ounce (30 cc.) of a 25 per cent suspension in water at intervals of 1 hour up to 3 or 4 times daily. This method usually follows the tube method in acute cases, and in cases requiring less drastic measures, may be used alone.

It is suggested that this drug is particularly advantageous in cases which do not respond well to the usual medical treatment because of hypersecretion or night secretion, in cases complicated by nephrolithioses, and in patients who develop alkalosis while receiving alkaline powder ³⁰

COLLOIDAL CALOMEL OINTMENT

Cornbleet, Slepvan and Ebert³¹ introduced the new colloidal ointment They developed calomel in which the particles are small-0 5 micron in diameter This calomel in aqueous suspension with gelatin was incorporated into the ointment base, and the new colloidal ointment produced an inhibitory ring from 3 to 6 times as broad as did the official calomel ointment. Its greatest therapeutic value was in impetigo contagiosa, clearing the eruption in an average of one-third to one-half the time required by ointments of ammoniated mercury Seborrheic eczema behind the ears, which is often quite resistant to treatment, was favorably influenced by applications of colloidal calomel ointment It improved leg ulcers aggravated or continued by a secondary pyogenic infection.

CONVALLAN

Convallaria majolis, or lily-of-the-valley, has been known for many years as a cardiac tonic and diuretic. However, convallaria has played a very small rôle in the therapy of cardiac disease because the preparations available have not been standardized, and are often inert.

Marvin and White showed that the activity of convallaria is due to certain glucosides which resemble digitalis. W. Kasser isolated a crystalline glucoside of convallaria by extraction with chloroform and named it convallatoxin. An assay of this substance showed that it contained 3 million frog doses per gram. Straub described an extract prepared by testing an aqueous solution of convallarıa with colloidal ıron hydroxide and concentrating the filtrate to a powder. This extract he named "convallan." Straub's convallan was found to consist of 20 per cent convallatoxin and 80 per cent "convallamarin complex." Physiologic assays showed that convallan contained 4000 to 8000 frog doses per gram.

Von Bergmann studied the pharmacologic properties of convallan and found that its activity, as measured in frog doses, showed that it stood between digitalin and strophanthin in therapeutic effect, but was much less toxic than either

These findings were confirmed by Buttner, who found from his clinical studied that the minimum effective dose was 3000 frog units, that the maximum dose which could be employed was 20,000 units, and that doses of 12,000 frog units may be administered daily with safety Buttner also found that convallan had little, if any, cumulative action, and that it may be given before or after digitalization with complete safety.

Buttner also noted that the pharmacologic action of convallan in large doses was essentially the same as that of digitalis and strophanthin. However, small doses produced a remarkable diuretic effect without causing heart block or increasing the degree of an already existing block.

This interesting observation suggested, to Major and Leger,³² its use in patients suffering from cardiac failure associated with varying degrees of heart block. The dosage employed in their cases was determined by the pharmacologic effect obtained in the individual patients, and averaged 2000 to 3000 frog doses daily.

The impression of these authors is that convallan can be employed, often with much benefit, in cases of heart block, or bundle branch block with cardiac failure in which the administration of digitalis is not advisable

DESOXY-CORTICOSTERONE ACETATE

Cleghorn, Fowler and Wenzel33 report the use of desoxy-corticosterone acetate in 9 cases of Addison's disease and in all, there was undoubted clinical improvement They summarized the patients as having increased sense of well being on desoxy-corticosterone acetate. Blood pressure and blood findings were restored approximately to normal It has a definite advantage in that it can be given in small injections and is less painful than cortin. Because of the slow rate of absorption in the oily solution in which it is contained, it is of little use in times of severe crisis and with severe vascular collapse They note that cases of local reaction with fever, following the use of desoxy-corticosterone acetate in oil, have been reported, but in their opinion this was due to accidental subcutaneous injection. They also note that there is some evidence that it does not provide complete replacement therapy.

Thorn³⁴ in an editorial in the *Annals* of *Internal Medicine* mentions that prolonged hormone therapy may be obtained by planting subcutaneously tablets of crystalline desoxy-corticosterone acetate in patients with Addison's disease. The hard tablets, being only slightly water soluble, are absorbed slowly and provide a supply of hormone for several months.

DIGITALIS

One of the not uncommon questions which arises, in the treatment of cardiac diseases, is that dealing with the use of digitalis in patients with pre-existing heart block.

Blumgart and Altschull³⁵ have made a very helpful survey in this respect

Nineteen patients ranging in age from 15 to 72 years were studied. Congestive heart failure was present in almost all subjects. In 3, a varying 2 to 1 and 1 to 1 relationship between auricular and ventricular contractions existed In most of the patients prolongation of the P-R interval was due to coronary sclerosis; in the others, rheumatic heart disease was present.

A standardized preparation of digitalis was administered in doses calculated on the basis of body weight; in accord with general practice, somewhat less than the full Eggleston dosage was administered.

The results demonstrate that digitalis in doses sufficient to induce therapeutic effects may be given to patients with partial heart block without causing interference with the orderly passage of impulses from the auricles to the ventricles. The dosages employed were those usually employed in treating patients with congestive failure in the hospital; the adequacy of the amounts used was indicated by the therapeutic response.

The results of this study show that while digitalis and organic heart disease each result in interference with auriculoventricular conduction, these factors do not reinforce each other and their simultaneous presence does not lead to an additive effect.

When doses in therapeutic amounts, as in this study, are utilized, the presence of partial heart block does not constitute a contraindication to the use of digitalis.

DIHYDROTACHYSTEROL

Rose and Sunderman³⁶ report on 5 cases of parathyroid deficiency following thyroidectomy, treated with dihydrotachysterol They found it to be highly effective in increasing the concentration of serum calcium and in relieving the symptoms of parathyroid deficiency. Also, excessive doses were capable of producing hypercalcemia with toxic symptoms. The authors note that the diffusable and the nondiffusable fractions of the serum calcium share about equally in the rise in concentration of total serum calcium following dihydrotachysterol.

Hurxthal and Claiborne⁸⁷ used dihydrotachysterol (A T. 10) in 6 cases of tetany with good results. The initial dosage ranged from 3 to 5 drams (12 to 20 cc) and reduced to 15 to 45 minims (1 to 3 cc.) daily. Principally because of the expense, the authors recommend using calcium lactate alone in the milder cases

Probably dihydrotachysterol acts by increasing the absorption of calcium from the enteric tract But Greene and

Swanson³⁸ point out it also increases the urinary excretion of phosphorus, as does parathormone. Hence the dosage can be kept down with a diet high in in calcium and low in phosphorus. This best can be achieved by prescribing a low calcium, phosphorus diet supplemented by calcium salts.

DILATIN (EPANUTIN, SODIUM DIPHANYL HYDANTOINATE)

This drug has been investigated particularly for its value in epilepsy, by Davidson and Sutherland,³⁹ in England, and Kimball and Horan,⁴⁰ in this country.

The experience of these authors indicates that the drug is undoubtedly 1 of the most potent anticonvulsants thus far used. Its use is greatest in the younger and better preserved patients because of its toxic effects, particularly on individuals after the fourth decade.

The average dose employed is about $\frac{2}{3}$ grain (0.04 Gm.) daily. Toxic effects include headache, giddiness, nausea, anorexia, and ataxia and skin rashes

The outstanding favorable results of the use of this drug are, in most cases, a definite improvement in mental faculties, lack of hypnosis, and its anticonvulsant effects.

ESTROGEN

That most difficult problem of chronic pruritis vulvae associated with leukoplakic and kraurotic changes of the labial skin is attacked anew by Kevorkian. He thoroughly cleans the vulva and epipubic and perineal skin, and then thoroughly massages with "estradiol" in sesame oil. "Estradiol" is estrogenic material in lanolin salve—15 minims (1 cc.) (60,000 international

units) is used for each inunction at 2- to 6-day intervals. Excellent results were reported in a group of 4 cases.

GENOSCOPOLAMINE

The use of genoscopolamine in parkinsonism is described by Scharf and Manong.⁴² Apparently, genoscopolamine possesses the properties of the alkaloid from which it is derived, but is much less toxic The authors tested it on 22 cases of parkinsonism of long standing. The patients were gradually withdrawn from their former medication and then genoscopolamine in the form of granules was administered Each granule was equivalent to $\frac{1}{120}$ grain (0.5 mg.). The usual optimum dose proved to be around 2 granules 3 times daily. A striking change was the disappearance of the toxic symptoms of atropine and hyoscine such as flushed hot faces, dry throats, blurred vision, dizziness, nausea, anorexia, tachycardia, and restlessness. Genoscopolamine does not benefit arteriosclerotic parkinsonism

GOLD

Gold is again suggested as a therapeutic weapon in selected cases of arthritis

Snyder, Traeger and Kelly⁴³ have reported a series of 100 cases, which they summarize as follows:

"I. Gold may be given as gold sodium thiosulfate (sanochrysin) intravenously, or sulfydryl gold naphthyl trisulfocarbonium (aurocein) intramuscularly, without serious permanent injury in the great majority of patients, if reasonable precautions are observed These precautions include careful selection of patients, small initial doses and gradual increase in dosage, and constant vigilance for evidences of toxicity

"2. In the rheumatoid group, 24 out of 50 patients (48 per cent) showed definite clinical improvement according to our criteria. In the osteo-arthritic group, 9 out of 20 patients (45 per cent) improved, while in the mixed group, 8 of 22 patients (26 per cent) showed improvement. Of the entire group therefore 41 per cent showed some degree of clinical improvement following gold salt therapy. The criteria for improvement are discussed. Our percentages of successful results in cases refractory to usual methods of treatment were not as good as those reported by European workers, but their series included early and untreated cases of arthritis, many of which might have been cured by other methods of treatment.

"3. We feel that our clinical results would have been better had larger doses been employed, or had we used one of the stronger salts, but toxic reactions would have been more numerous and more alarming.

"4 In the present status of our knowledge, gold salt therapy appears to be too dangerous for general use It should be undertaken only when the case is refractory to the usual forms of treatment. The risk involved should be explained to the patient before treatment is instituted."

GUANIDINE HYDRO-CHLORIDE

Minot, Dodd and Riven⁴⁴ report 5 cases of myasthenia gravis to whom guanidine hydrochloride was administered with favorable results. In several of these the beneficial effects of prostigmine was beginning to wane. The drug can be used either alone or to enhance the effect of prostigmine. It can be administered by mouth or intravenously. The authors used a 2 per cent solution

in normal saline for intravenous use and ½2 grain per pound (10 mg. per kg.) of body weight was found to be safe and adequate dosage. They found a marked and sustained improvement in muscular function in their 5 cases. Gastrointestinal symptoms are apt to appear and can be controlled somewhat by atropine, but the authors recommend that the dosage be temporarily reduced or withheld. A definite, adequate explanation of its function cannot be promulgated.

HEPARIN

Heparin, first isolated in 1916, has finally been purified sufficiently to be used intravenously. Sappington⁴⁵ reports using it in 40 transfusions as the anticoagulant It was used in 2 ways, first in vitro to heparinize the drawn blood of the donor. Second, in vivo to heparinize the donor by intravenous injection. Seventeen transfusions were given by the former method, 23 by the latter. From 20 to 75 and even 150 mg. of heparin were added directly without ill effect. The donor's dose was usually 1 mg. per kilogram or about 1.5 cc. of the 5 per cent solution injected intravenously. Withdrawal of the donor's blood was begun 7 to 8 minutes after injection. No sequelae were noted. The only objection is the larger needle required, the smaller needles clotting after 300 cc are administered Perhaps the therapeutic effect of heparin may be of advantage in postoperative transfusions.

The mortality rate in mesenteric thrombosis is 85 to 95 per cent. But Murray and MacKenzie⁴⁶ in 6 cases with resection followed by treatment with heparin found no further thrombosis or gangrene.

The outlook of proven, established cases of subacute bacterial endocarditis

has heretofore been hopeless. Apparently the infection persists because the constant deposition of platelets and fibrin on the vegetation exceeds the rate at which the vegetation on the valve can be sterilized. Kelson and White administered a combination of sulfapyridine and heparin to 6 cases. They added a 10 cc. vial of heparin (10,-000 units) to 500 cc. of physiological saline and gave as uninterrupted drip day and night for 14 days. Two of their patients were only able to take the heparin for 11/2 hours because of untoward reactions. Two others could continue the infusion only 2 to 3 days because of fatal course of disease. Three were able to take the heparin for over a week and displayed striking improvement, being free from evidence of disease for 19 days, 8 days or 4 weeks. Friedman, Hamburger and Katz⁴⁸ also administered heparin to a case which terminated fatally. Although cognizant of the many theoretical dangers, especially hemorrhage in a hemorrhagic disease, the authors still feel further trial is warranted.

HYDROXYETHYLAPO-CUPREINE

Among chemotherapeutic weapons, found to be useful in combating pneumonia, is found the above drug, which has been investigated by Maclachlan, Johnston, Brachen and Crum.⁴⁹

These authors report that (1) the mortality figure in pneumococcic pneumonia in adults was greatly reduced in those cases receiving hydroxyethylapocupreine, (2) in comparing the mortality figures of their chemically treated cases, which were, of course, smaller in number, with the serum treated cases in Pittsburgh for the same types of pneumonia, during the same period of time,

almost identical results were observed; (3) the drug showed no evidence of disturbing vision.

Hydroxyethylapocupreine dihydrochloride was given in capsules by mouth, 15 grains (1 Gm.) every 3 hours day and night for 3 to 5 days. In some patients, it produced nausea and occasionally vomiting. However, in only a few cases was it necessary to discontinue the chemical for this reason. It may be that in the future the base or another salt will be used by mouth instead of the dihydrochloride. For intravenous use a monohydrochloride solution is given, each $1\frac{2}{3}$ ounces (50 cc.) containing 15 grains (1 Gm.) and this is injected into the vein every 3 hours. The intravenous solution is given slowly, from 7 to 10 minutes being taken for 50 cc. At this rate, there have been no reactions given rapidly, a weak rapid pulse may be noted with some fall in blood pressure. The authors have seen very few reactions of this kind and feel fairly certain that their cause is carelessness due to speed in the injection of the chemical Thrombosis of veins at the point of injection does occur at times, especially if the veins are difficult to enter, but is less with the monochloride than with the dihydrochloride.

INSULIN

Crystalline Insulin

Since the introduction of insulin specially prepared from zinc insulin crystals there has been some confusion regarding its rapidity and duration of action. Marble and Vartiainen⁵⁰ and Richette and Wilder⁵¹ made detailed studies comparing crystalline and amorphous (unmodified) insulin. Their conclusions were similar, that is the action of the 2 insulins is almost identical, both

being rapid although the crystalline may be a trifle prolonged. Since it is advisable to reduce the number of insulin injections to a minimum, crystalline insulin for quick action and protamine zinc insulin for delayed action would appear to be the 2 insulins of choice.

Protamine Zinc Insulin

One theoretical criticism of prolonged use of protamine zinc insulin is the frequency of postprandial glycosuria. Rabinowitch, 52 using a carefully controlled series of cases followed with plasma cholesterols, came to the conclusion that the postprandial glycosuria in diabetes treated with protamine zinc insulin. when associated with a normal blood sugar in the fasting state, is not harmful. Mosenthal⁵³ followed 114 diabetics who had been taking protamine zinc insulin for over 6 months and found only 4 failures. The incidence of acidosis and coma was less frequent, and with discretion in the dosage hypoglycemic attacks were no more frequent. Pollack and Dolger⁵⁴ summarize the advantages of protamine zinc insulin as follows: (1) Single injection daily for patients, (2) complete elimination of transient ketonuria, (3) closer approximation to the normal carbohydrate metabolism, (4) decrease in the incidence of hypoglycemic episodes; (5) valuable as a supplementary agent in coma therapy; (6) improvement in postoperative control of diabetic patients, (7) obviate the absolute necessity of multi-feeding schedules, yet permits optional midnight snacks.

MALNUTRITION

Another favorable report of the use of insulin in nondiabetic nutrition was presented by Blotner⁵⁵ who followed 100 cases for from 1 to 8 years after the

insulin was discontinued. The average dose was 10 units 3 times daily about 20 to 30 minutes before eating. The period of treatment ranged from 3 weeks to 4 months. The usual gain in weight was 3 to 4 pounds for several weeks and then decreasing amounts thereafter. Finally the weight remained stationary. The average gain was 15 lb Biopsy showed the gain to be due to increased depth of subcutaneous fat.

Insulin has been used for nearly every condition existent by 1 person or another. Its use as an external dressing has been mentioned several times. Hunter⁵⁶ puts this gently to rest with a series of 10 cases—concluding that insulin is no more satisfactory as an external dressing than a similar solution of tricresol containing no insulin

IRON

Bethe, Gardiner and MacKinnon⁵⁷ point out that in 158 pregnancies a true anemia occurred in 54 per cent ascribe this to a deficiency or impaired utilization of iron. Hemoglobin values below 10 Gm per 100 cc. are never physiological and a low color index indicates a lack of available iron. A red count below 3,500,000 would suggest a co-existing protein deficiency. The authors recommend inorganic ferrous compounds as the most effective and least irritating, and suggest they be used throughout pregnancy In the treatment of its more severe macrocytic anemia a diet containing 15 Gm. of protein per kilo is suggested

MALE SEX HORMONE

The many conflicting reports on the male sex hormone makes a more exact

definition of its clinical use desirable. One must remember that there are 2 types of hormone therapy now available in hypofunction of the tests (1) stimulation with gonadotrophic material and (2) substitution therapy with male sex hormone. In clinical work the propionic acid ester of testosterone (testosterone propionate) is being used. Thompson and Heckel⁵⁸ outline its present status as follows. (1) Testosterone propionate is an important therapeutic agent; (2) its administration represents primary substitution therapy, in contrast to stimulation therapy with gonadotrophic material, (3) its use is indicated in conditions in which the testis is incapable of responding to stimulation; (4) its most important application is in the treatment of castrated and eunuchoid persons: (5) it may cause a marked reduction in the number of spermatozoa in normal men. For the reason it is contraindicated when the testis is capable of normal function and it is probably of no value in the treatment of sterility, (6) although it is as effective as the gonadotrophic factor of pregnancy urine in undescended testis, treatment with the latter is to be preferred because of possible injury to the testis with male sex hormone; (7) it does not appear to be effective in the treatment of benign prostatic hypertrophy; (8) in the treatment of impotence it is indicated only in those cases in which the natural production of male sex hormone is deficient; (9) its value in reviving the sexual, mental, and physical vigor of old men is still to be determined.

MAPHARSEN

Rein and Wise⁵⁹ present a study based on 2342 injections of 113 patients. They found that the majority of patients in this series tolerated mapharsen therapy

well and presented no serious untoward reactions. Among the 113 patients, 16 had mild gastrointestinal reactions such as nausea, 11 had nausea and vomiting, 4 complained of mild headaches and attacks of dizziness, 3 had pruritis, and 1 developed herpes simplex. Of these 113 patients, 10 had similar reactions with other arsenical preparations, 15 developed the more serious delayed reactions, 2 had chills and fever, 4 developed generalized erythematous eruptions, 5 had an exacerbation of a pre-existing dermatitis, 2 developed fixed eruptions, 1 complained of precordial pain, 1 developed albuminuria Mapharsen had to be discontinued for a short time in some of these cases. In 3 cases it had to be stopped entirely. The authors concluded that mapharsen is therapeutically adequate to control early infectious syphilis, producing rapid sterilization of active reactions. Also, that the majority of syphilitic patients treated by physicians in private practice are in the latent asymptomatic stage Mapharsen possessing relatively lower toxicity is preferable in such cases to other drugs which have a greater tendency to produce untoward reactions

METRAZOL

Cohen⁶⁰ reports the outcome after 6 months in 146 schizophrenic patients in whom daily treatment with metrazol had been carried out. It was found that the stability of the therapeutic effect as compared 1 month and 6 months after cessation of treatment depended largely on whether full remission had occurred For those patients who had achieved full remission, 89 per cent remained in this fortunate state after 6 months. On the other hand, of those patients who had shown much or slight improvement after 1 month, only 30 per cent retained the

improvement after 6 months. The conclusion may therefore be drawn that anything short of a full remission must be considered pessimistically so far as this therapy is concerned.

Bennett⁶¹ presents a follow-up report of metrazol convulsive shock therapy in 61 depressives and 9 manic cases. Of 61 depressed patients, 28 obtained a full remission lasting from 3 to 18 months. 32 obtained a social recovery, and 7 relapsed Four of these were improved again in a second course of treatment, 1 remained unimproved, and 1 committed suicide. Fifty-seven of the 61 patients obtained rapid improvement with termination of the depression by metrazol shock therapy. Over 50 per cent of these patients were past 45 years, and 42 per cent were past 55, the oldest was 68.

Four of the 9 manic states obtained a full remission lasting from 3 to 18 months, 4 obtained a social remission, and 2 relapsed. The average number of shocks given every 2 to 3 days for the depressives was 67, with an average period of 3 weeks under treatment. The average number of treatments for the manics was 4. The average duration, 16½ days. The author concludes that convulsive shock therapy in spite of certain hazards is an indicated therapy in chronic depressive and manic affective states.

NEOPRONTOSIL

Compounds of the sulfamido type continue to share the limelight in medical therapeutics. During the past year neoprontosil has been advanced by Brown, Herrell and Bargen⁶² as a therapeutic weapon in the treatment of chronic ulcerative colitis.

Neoprontosil was chosen for use in these cases because of its relative lack of

toxicity. Although minor degrees of malaise, fatigue, and headache were noted at times during the treatment, the symptoms were never of a degree sufficient to necessitate withdrawal of the drug and but rarely were of a nature requiring a reduction of the prescribed doses There is occasionally some tendency to local irritation of the bowel, cramps, and diarrhea may occur at times when large amounts of the drug are given, for instance, amounts in excess of 82 grains (55 Gm) daily. It is felt that an explanation for this irritation rests on the probability that the bowel is receiving larger amounts of the drug than it is able to absorb and that some local irritation is thereby produced.

The average dose was 82 grains (5 5 Gm) daily, but was varied according to the reactivity of the patients.

It appears that slightly over 40 per cent of the patients treated obtained excellent results, another 30 or more per cent obtained fair results, and the rest poor

The authors express themselves as being exceedingly anxious not to create the impression that neoprontosil is a specific remedy for chronic ulcerative colitis. However, it is reasonable to deduce from the results herein reported that the use of this drug and the comparatively encouraging clinical responses amply justify the use of neoprontosil (oral) in the treatment of chronic ulcerative colitis.

NOVOCAIN

Novocain has many uses. One of the most recently described is its use in thrombophlebitis 63

The symptoms of thrombophlebitis probably result from arteriospasm, set up by a vasomotor reflex originating in the thrombosed venous segment. By block-

ing the sympathetic ganglia with novocain, this reflex can be broken.

Usually, within 24 hours after the treatment, the temperature declines generally reaching normal within 72 to 96 hours. The swelling of the extremity begins to diminish within 24 to 48 hours and usually within 7 to 10 days has disappeared completely. In over 50 per cent of the cases the extremity has returned to normal size within 4 days after the beginning of treatment. In contradistinction to the usual 6 to 8 weeks of bed rest, there is a convalescence of but 2 weeks, every patient being able to walk out of the hospital within or shortly after that period of time

Lumbar, cervicodorsal, and stellate ganglia can all be readily injected with a simple technic. Most instances of thrombophlebitis occur in the lower extremity, hence the lumbar ganglia are more frequently blocked

Technic of Injection of Lumbar Ganglia—Skin wheals are raised with 1 per cent novocain at points approximately 2 to $2\frac{1}{2}$ fingerbreadths lateral to the upper part of the spinal process of the first to fourth lumbar vertebra. These points are directly over the transverse processes of the corresponding vertebra. A 20- or 22-gauge needle 8 to 10 cm. in length is used. The needles are inserted vertically through each wheal until the transverse process of the corresponding vertebra is reached, a distance of 4 to 5 cm. The direction is then changed slightly either superiorly or inferiorly and is pointed slightly toward the mid-The needle is then inserted for another $2\frac{1}{2}$ fingerbreadths so that the point impinges against the anterolateral surface of the body of the vertebra Five cc. of 1 per cent novocain are injected. Before injection, aspiration should be done to avoid injection into a blood vessel In a few minutes after a satisfactory

injection, the extremity on this side becomes warm and dry.

Very similar technics are used for injecting cervicodorsal and stellate ganglia.

OXYGEN

Of the many uses of oxygen, attention recently has been called to 2 which are of utmost importance. The first of these is the use of 95 to 98 per cent oxygen in the treatment of abdominal distention and certain other conditions, and is reported by Congdon and Burgess.⁶⁴

This method depends on the fact that the inhalation of almost pure oxygen so reduces the nitrogen content of the alveolar air that nitrogen passes from the blood plasma into the alveoli, and that the reduction of nitrogen tension in the plasma, which results, causes in turn a passage of nitrogen into the blood from any area in which nitrogen is trapped, as in small bowel distention or in subcutaneous emphysema It has previously been demonstrated that the gas in distention of the intestine consists principally of either nitrogen or hydrogen; in most cases, the former Furthermore, Fine and his colleagues showed that air injected subcutaneously soon loses its oxygen content, nitrogen remaining They demonstrated in experimental animals that absorption of this nitrogen can be accomplished by the inhalation of 95 per cent oxygen. Clinically they applied the method to patients with gaseous abdominal distention, and also to those with distention of the cerebral ventricles with air resulting from the making of encephalograms, they have reported considerable success in the control of these conditions

In the work of Congdon and Burgess, 40 cases of abdominal distention and 3 cases of subcutaneous emphysema treated with 95 to 98 per cent oxygen are reported. Of the patients with abdominal distention, 25 were strikingly benefited, 5 questionably benefited and 10 uninfluenced. Of those with emphysema, all had satisfactory results. Following encephalography, the routine use of the method has appeared to prevent severe headaches.

These authors point out that when this treatment is used, it should be considered as an emergency measure to be applied only when simple means fail, because there is ample evidence to indicate that exposure to such concentrations of oxygen may be harmful.

Alvarez⁶⁵ has reported rather marked success in relieving migraine headaches by having patients inhale 100 per cent oxygen for brief periods, through the medium of the new B L. B. inhalation apparatus devised by Boothby, Lovelace and Bulbulian His series is small, but so striking that it seemed worth while to place the method before the profession at large.

PAPAVERINE

Mulmas, Shulman and Mufson 66 studied the effect of papaverine on 5 patients with Raynaud's disease. They gave papaverine hydrochloride intravenously in doses of from 1 to 2 grains (65 to 130 mg) 3 times a week, usually before and after histamine iontophoresis. These large doses of papaverine seemed to depress somewhat the sensorium of the patients but never to such an extent that they could not carry on immediately after the injection At no time was there any evidence of desire for the drug other than for the relief it afforded the symptoms. After a week or 2 of treatment, the condition would improve sufficiently so that need of relief was not so obvious to the patient

PENTONUCLEOTIDE

In an analysis of 390 cases of agranulocytic angina, Jackson and Tighe⁶⁷ have concluded that pentonucleotide therapy, in doses of at least 1½ ounces (40 cc.) daily, is the most promising form of specific therapy in this disease.

They further point out that neither transfusions nor x-ray therapy seemed to alter the mortality rate. Treatment by yellow bone marrow extract, leukocytic cream or adenine sulfate has not been widely enough reported upon to permit any accurate conclusions as to their worth. Because of the low mortality in the cases so far reported, these latter measures deserve further trial

PENTOTHAL SODIUM

Ruth, Tovell, Milligan and Charleroy⁶⁸ made a critical survey of pentothal so-They emphasize that the contraindications are specific. It should rarely be used for patients under 15 years of age. Cardiac dysfunction to the point of dyspnea, varicosities central to the point of injection, manipulations disturbing pharyngeal and laryngeal reflexes, a definite deviation from normal in the oxygen carrying capacity of the blood, and gross hepatic damage are all recognized contraindications The authors emphasize that special care should be taken to maintain an efficient air way and one should always be prepared to administer oxygen by inhalation if necessary. The maximal dose of 15 grains (1 Gm) rarely needs to be exceeded. It should be administered by a competent anesthetist In their hands the drug produces satisfactory results No postoperative pulmonary complications were encountered and no operative fatalities occurred

Weinstein⁶⁹ describes the use of pentothal sodium rectally in 164 cases The

dosage used was 15 grains (1 Gm.) for each 50 lbs. (22.7 kg.) of body weight. Technic consisted of dissolving the required amount of pentothal sodium in 1 ounce of distilled water and instilling it into the rectum by syringe through a catheter or by the gravity method with a funnel. Complete absence of excitement, increased relaxation, and a minimum need for a supplementary anesthetic were noted Short basal anesthesia is secured with no depression of the blood pressure and only slight depression or not change in the respiration. The recovery is rapid without excitement and the patients have a complete absence of disagreeable symptoms. There was no mortality.

Bourne and Pauly⁷⁰ used pentothal in 60 cases and thioethamyl (the sulfur substitution of amytal) in 40 cases of labor. They found that the degree of analgesia was fairly good following the administration of pentothal and only moderately good after thioethamyl. Amnesia was not nearly so marked as one would like with either drug. No harmful effects were noted in the mothers or babies

POTASSIUM CHLORIDE

Excellent clinical results in the treatment of urticaria and hay fever by the administration of potassium salts by mouth have been reported by Rusk and Kenamore⁷¹ and by Bloom ⁷² This therapy is apparently based on the pharmacologic similarities of potassium and adrenalm and on D'Silvos' discovery that the injection of adrenalm in animals is attended by a rise in the serum potassium due to the liberation of potassium from the liver

Harley,⁷³ of London, reports a series of cases including hay fever, allergic rhinitis, asthma, urticaria, and eczema, in which he used oral potassium chloride

His conclusions were in accord with the general impression, "Oral potassium chloride therapy, in the dosage employed, failed to produce a significant degree of improvement in a group of 43 allergic patients."

PROSTIGMIN

Viets and Schwab⁷⁴ treated 44 cases of myasthenia gravis in a period of 2½ vears with prostigmin bromide taken by mouth and supplemented with ephedrine sulfate, potassium chloride, and occasionally guanidine. Guanidine increased the effectiveness of prostigmin in 8 of 25 cases In 4, the results were good Seventeen other patients, however, failed to respond to guanidine. Of 15 patients using potassium chloride with prostigmin, there was a decided benefit in 10 Vitamin and endocrine treatments were not helpful With the oral prostigmin, large doses of the drug were necessary in the severe cases—from 10 to 20 pills of 14 grain (15 mg) each daily Others required only small doses, ½ grain (75 mg), spaced widely through the day Once the dosage was regulated, no change was necessary for months and no increased tolerance or disagreeable effect from the accumulation of the drug was observed. Of the 44 patients treated in this way, 31 have taken the drug for more than 1 year and 9 for more than 2 years. There have been only 5 deaths, and in 7 cases there were complete remissions. The authors conclude that oral prostigmin bromide supplemented as above is now the most efficient form of treatment for myasthenia gravis available

QUININE

Quinine has been suggested by Hassin⁷⁷ for use in dystonia musculorum deformans. He reported observations on

several cases of this disease and concluded briefly: "The muscular restlessness in dystonia musculorum deformans is, as in Thomson's disease (myatonia congenita), probably a disturbance of the muscle tone. Like myatonia congenita, dystonia markedly improves with quinine therapy. Large doses should be given, if possible; they are of decided benefit even in cases of so-called spasmodic torticollis, which is also known as torsion spasm (a partial manifestation of dystonia)." Doses up to 30 grains (2 Gm) per day are suggested

QUINIDINE

Considerable variance of opinion exists regarding the advisability of attempting to restore normal cardiac rhythm by the administration of quinidine in cases of auricular fibrillation Smith and Boland⁷⁵ present a paper based on the results obtained in 41 consecutive cases of auricular fibrillation In most cases, 5 grains (03 Gm.) of quinidine were administered every 3 hours and $\frac{1}{40}$ or $\frac{1}{30}$ grain (15 or 2 mg) of strychnine sulfate was administered 3 times a day. The total amount of quinidine that was administered varied between 10 grains and 2620 grains (06 and 1698 Gm) before normal cardiac rhythm was established Nausea, vomiting, diarrhea, weakness, and palpitation developed in 9 per cent of the cases In no case did embolism or arterial occlusion occur while the patient was being treated. Sudden death occurred in 3 cases Normal cardiac rhythm was reestablished in 80 per cent of the cases The authors believe that quinidine is especially indicated when the patients are young persons who have idiopathic auricular fibrillation but who do not have any other evidence of heart disease. The patients of the next group who should

receive quinidine are those who have a minimal amount of heart disease and who have auricular fibrillation only a short time Quinidine should be administered in cases in which auricular fibrillation is due to hyperthyroidism but not associated with any significant evidence of any organic heart disease. The greatest danger in giving quinidine is the possible occurrence of sudden death. In well selected cases, the danger appears slight.

Weisman⁷⁶ reports favorable clinical experience with some 200 cases of auricular fibrillation treated at the University of Minnesota They believe that quinidine should be given in small doses to start with—about 1½ grains (0.1 Gm.) and then increased daily and very slowly. Patients should be thoroughly digitalized before therapy is commenced

RHUS TOX ANTIGEN

In September, 1938, Caulfeild⁷⁹ reported the use of a poison ivy extract in oil for the specific diagnosis and treatment of ivy poisoning. This series, while brief, gave some encouraging results, which he summarizes as follows:

- "1 The extract from the poison ivy plant, termed 'rholigen,' suitably diluted for patch testing, has been found of value in the differential diagnosis of dermatitis regarded as possibly due to contact with poison ivy
- "2 Observations have been presented in support of the conclusion that the intramuscular injection of this extract in increasing amounts actively influences the severity and duration of an attack of poison ivy dermatitis
- "3. Following an adequate series of intramuscular injections of this extract all individuals susceptible to poison ivy dermatitis have shown a greatly reduced

(with a questionable reservation in 1 case) or even a negative quantitative patch test.

"4. Practical clinical results, based upon re-exposure to the same environment have confirmed the theoretical conclusion that a satisfactorily reduced quantitative patch test coincides with clinical immunity to ordinary contact with this weed."

The extracts commonly used in work of this kind are dilutions of 1 to 10,000 and 1 to 1000. The dosage is not fixed but is graded according to the patient's reactions to the patch test itself and intramuscular injection for therapy.

Recently Zisserman and Birch,⁸⁰ working with a group of Boy Scouts in Philadelphia, and using similar extracts, reported less favorably.

They pointed out that "the massive standard dose method of rapid prophylaxis for poison ivy dermatitis is not generally beneficial and actually makes many patients more susceptible. Its routine use is contraindicated."

They further point out that although there may be some therapeutic benefit from rhus extract given intramuscularly during an attack of poison ivy, the problem requires further study with suitable control; benefits are by no means always obtained

STAPHYLOCOCCIC ANTI-SERUM TYPE A

One of the most baffling conditions requiring active therapy is staphylococcal septicemia. Among the therapeutic weapons designed to combat this condition is a rabbit serum reported favorably, but conservatively, by L. A. Julianelle 81

This investigator has divided staphylococci into 2 great groups, called Types A and B. The differentiation of the types was established primarily by immunolog-

ical and chemical differences between the intracellular polysaccharides extracted from the respective organisms, and secondarily by the biological distinction that Type A strains are derived from pathogenic conditions, while Type B strains are apparently saprophytic.

It is difficult to standardize such treatment But, in general, using the serum prepared according to the method reported in Julianelle's paper, the method of treatment was briefly as follows: One cc. of antiserum in 10 cc of saline is injected intravenously as a test dose within an hour no significant changes occur in blood pressure (reduction of 15 mm. or more) and respiration (15 beats or more per minute), 50 cc of serum diluted in saline may be given intravenously, the injection being made slowly, with adrenalin ready for immediate use if indicated The treatment from then on is based on the clinical signs and the record of blood cultures Injections may be repeated once or twice daily with 25 or 50 cc quantities, and the injections continued as long as the clinical indications demand additional serum

Julianelle⁸¹ reported 71 patients with staphylococcal septicemia from organisms of the above type. All were treated with Type A antiserum and whatever supplementary measures were indicated (e.g., surgical drainage, blood transfusions, etc.) The untoward reactions ascribable to the serum were mild, and in 4 patients the treatment was followed by serum sickness. Of these patients, 7 recovered and 10 died.

STROPHANTHIN

Careful observation of toxicity and clinical value of strophanthin was made by Brams, *et al.*,⁸² with the following conclusions:

- 1. Single intravenous injections of $\frac{1}{120}$ or $\frac{1}{80}$ grain (0.5 or 0.75 mg.) of strophanthin K in normal persons failed to produce significant clinical or electrocardiographic evidence of toxicity
- 2. Similar absence of toxicity was noted after $\frac{1}{200}$ or $\frac{1}{120}$ grain (0 3 or 0.5 mg.) in patients with severe cardiac failure, the majority of whom also had hypertension and regular rhythm.
- 3. Continued injections of $\frac{1}{200}$ grain (0 3 mg) daily for as long as 24 days consecutively also failed to produce clinical or electrocardiographic evidence of toxicity in patients with cardiac failure.
- 4. Accessory measures, such as sedation or diuretics, were sometimes necessary as with digitalis
- 5. The therapeutic results of strophanthin seemed comparable in every way to those obtained by adequate digitalization when digitalis is given orally
- 6. Strophantin is a safe and rapidly acting drug when used in proper dosage and in suitable patients. Its properties are practically those of digitalis but its speed of action and safety render it an ideal drug in acute cardiac emergencies, in marked congested failure where oral digitalis is absorbed with some uncertainty, and in those instances where one wishes to try another drug when digitalis has failed

SULFANILAMIDE

Sulfanilamide is now rapidly finding its true place in the scheme of medicine However, it still remains the most alive subject in contemporary medical literature and it would be impossible in a brief space to quote the innumerable articles on the subject. The actual mechanism of the drug remains debatable. Apparently it is bacteriostatic, allowing the natural immunity defenses of the body to act. King has been able to demonstrate that

it certainly is bacteriostatic for all types of beta streptococci, and that this effect varies directly with the concentration of the drug and inversely with the number of bacteria. Studies on toxicity are virtually meaningless because the toxicity varies with different species of animals.

Agranulocytosis, at first thought to be a very uncommon complication, is rearing its head more frequently in case reports, at times proving fatal. Numerous cases of fatal hemolytic anemias likewise are reported. It is interesting to note the high incidence of syphilis as a complicating factor in these latter cases.

Various forms of beta streptococci infections appear to be the particular field of sulfanilamide. It also has proven itself of definite value in gonorrhea and meningococcic meningitis Gonococcal arthritis also responds, but therapy has to be prolonged or recurrences will occur. As a urinary antiseptic, it has proved efficient. Those cases caused by B coli and B. proteus respond most favorably, while no response at all is obtained against S. fecalis To a lesser extent than previously, it continues to be used against all forms of infections. Scattered reports would indicate that it helps undulant fever, scarlet fever, ulcerative colitis, trachoma, severe corneal ulcers, and measles Effectiveness against the staphylococcus and pneumococcus has not been demonstrated. Mortality in generalized peritonitis from appendicitis has been markedly cut

SULFAPYRIDINE

Chemotherapy continues its onward march and in the forefront one finds sulfapyridine, which continues to attract increasing attention. The end has not yet been approached, and no one may hazard a guess as to the limits of useful-

ness to which this compound, and its relatives, may be put.

The literature is overcrowded with reports of investigators, most of whom are enthusiastic, some reserved, but all increasingly hopeful. Its successful use has been reported in trachoma, 83 gonorrhea, 84 staphylococcus aureus bacteremia, 85 Friedlander's septicemia, 86 subacute bacterial endocarditis (with heparin), 87 granuloma venereum, cerebrospinal fever, 88 influenzal meningitis, 80 pulmonary tuberculosis, 90 and many other conditions. The most noteworthy efforts are, of course, in the field of the pneumonias.

An excellent study of the use of sulfapyridine in pneumonias is presented by Pepper, Flippin, Schwartz and Lockwood. These authors treated 400 cases of typed pneumococcic pneumonia, according to the dose schedule recommended by Evans and Gaisford. An initial dose, by mouth, of 30 grains (2 Gm.) was followed by 15 grains (1 Gm.) every 4 hours until a total of % oz. (25 Gm) had been given. Occasionally alteration of this schedule was required, but such was the average course.

This series presents a mortality of 7 per cent Of the 400 cases, 197 were caused by the first 3 types, with a mortality of 58 per cent in 104 cases of Type I pneumonia, 67 per cent in 30 cases of Type II pneumonia, and 16.4 per cent in 67 cases of Type III pneumonia

Toxic reactions noted were nausea (53 per cent), vomiting (418 per cent—36 per cent troublesome, 5.8 per cent severe), dermatitis (05 per cent), acute hemolytic anemia (025 per cent), leukopenia (0.5 per cent), drug fever (05 per cent), and psychosis (1 per cent). Complications were remarkably few.

This experience is typical of the majority of investigators in this field, and

tends to indicate that sulfapyridine is an effective therapeutic agent in the treatment of pneumococcic pneumonia. This preparation undoubtedly has great potentialities in this and other fields. Only time will show us the limitations and values of such a great chemotherapeutic agent.

TETANUS TOXOID, ALUM PRECIPITATED REFINED

This substance is of particular value in the immunization of allergic subjects against tetanus This was ably demonstrated by Gold.92

The results of these investigations indicate that allergic subjects can be immunized safely against tetanus by means of 2 injections of 15 minims (1 cc) each of alum precipitated toxoid, given 90 days apart The response of allergic individuals to such a basic course of immunization is the same as that elicited in nonallergic persons

If an injury occurs during the interval of time that elapses between the injection of the 2 doses of toxoid and for a week or 2 following the second dose, one must resort to the prophylactic injection of 1500 units of tetanus antitoxin for protection against tetanus

The antitoxin protection that develops in allergic subjects following the basic course of immunization is variable in duration as in nonallergic individuals This necessitates the injection of a third or "repeat" dose of alum precipitated toxoid (15 minims-1 cc.) upon the occurrence of an injury This will bring the antitoxin content of the blood up to a protective level One-tenth of a unit or more of tetanus antitoxin can be demonstrated in the blood in 4 to 5 days following the "repeat" injection of toxoid.

THYROID EXTRACT

Aisner and Dorsey⁹³ report an interesting case of complete heart block resulting from overdosage with thyroid extract. For 3 years before admission, the patient was taking thyroid extract because of obesity associated with a low basal metabolic rate For 5 weeks previous to her illness, she had been taking 4 or 5 2-grain tablets of desiccated thvroid extract daily. This case represents an excellent illustration of what may be expected from the uncontrolled use of thyroid extract in the treatment of obesity.

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OPHTHALMOLOGY

By Conrad Berens, M.D., and Joshua Zuckerman, M.D.

ANISEIKONIA

Aniseikonia may result from anisometropia, the wearing of glasses of different magnifying power for each eye, and from asymmetric convergence, according to W. B Lancaster. Compensation for aniseikonia is limited as compared with amplitude of accommodation or amplitude of fusion Uncompensated aniseikonia usually results in suppression.

Beneficial results have been obtained from eikonic lenses but some of these results have been attributed to suggestion or psychotherapy, and to the production of anisophoria resulting from the supposed prismatic effect. Moreover, asymmetric convergence normally produces greater aniseikonia (compensated by increase in the size of the image of the adducting eye) than many of the cases of aniseikonia which usually produce symptoms.

ANTERIOR CHAMBER

Aqueous

From an investigation of the chemical equilibrium of the interstitial fluids and the aqueous humor, J. D. Robertson² concludes that the aqueous is a specialized fluid produced for a specific purpose. It is not a simple protein-free ultrafiltrate or dialysate of the blood plasma

Epithelialization

X-ray Treatment — K. Ascher³ reports that roentgen therapy resulted in thinning and eventual disintegration of an epithelial downgrowth into the ante-

rior chamber. Ascher applied a total of 1800 r in 5 doses at intervals of from 4 to 7 days. The eyeball remained normal.

ASTHENOPIA

F. C. Cordes and D. O. Harrington⁴ report 82 cases of asthenopia which were attributed to a deficiency of vitamin A as determined by the Bio-Photometer. It is interesting to note that only 22 per cent of these cases revealed a history of night blindness. After the daily administration of 30.000 units of carotene in oil, 79 per cent of the cases were completely relieved, and 12 per cent were partially relieved from their symptoms. Asthenopia resulting from vitamin A deficiency is usually characterized by chronic conjunctivitis, photophobia, fatigue of the eyes, especially at night, difficulty in reading for more than 20 ininutes (sometimes associated with momentary blurring of vision) and headache after driving or after attending the movies

BLEPHARITIS

Error of Refraction—E. J. Somer-set⁵ investigated the significance of errors of refraction in 300 cases of chronic blepharitis. He found that blepharitis occurred as frequently in normal children as in those who had astigmatism and that in uniocular cases of astigmatism, blepharitis did not occur more frequently in the eye which was astigmatic.

Treatment—Excellent results in 104 cases of various types of blepharitis fol-

(434)

lowing treatment with *lysozyme* are reported by M. S. Natanson.⁶

BRUCELLOSIS

Ocular Complications — Four cases of brucellosis (undulant fever) in which ocular complications occurred are reported by J. Green. He has found that almost any part of the eye may be affected. A serum for the treatment of the acute stage and a vaccine for treatment of the chronic stage, have been developed.

CHOROID

Detachment

Six cases of detachment of the choroid following cataract extraction have been reported by P. Bonnet and E. Grandclement.⁸ Reattachment was spontaneous.

Melanoma

A case of malignant melanoma of the choroid in a man, 26 years of age, is described by F. J. Pinkerton.⁹ When a posterior sclerectomy was performed to relieve the tension in a case of acute inflammatory glaucoma, the dark-red or black mass, which appeared in the wound, was found to be a melanoma. The eye was enucleated. Complete exenteration of the orbit was performed when the tumor recurred 11 months later. Metastatic involvement of the liver, 15 months later, resulted in death

Metastatic Hypernephroma

M. Fledelius¹⁰ reports a case of metastatic hypernephroma of the choroid located behind the ciliary body of the left eye. The left kidney had been removed 7 years previously.

CILIARY NEURALGIA

Treatment — W. Reitsch¹¹ observed that on closure and on movement of his evelids he developed a right-sided ciliary pain associated with an intense nasal catarrh and a painful spot near his right nasal bone at the border of the lateral cartilage. This neuralgia was alleviated by inserting larocaine sponges into the nose. He points out that the mucous membrane of the nose is supplied by the anterior ethmoidal nerve which is a branch of the ophthalmic nerve. In cases of ciliary neuralgia of obscure origin he recommends searching for sensitive areas in the nose and anesthetizing the mucous membrane of the nose even if a sensitive spot is not discovered.

CONJUNCTIVA

Burns

Treatment—The use of transplants from the labial mucous membrane in cases of chemical burns of the eye is advocated by O. Thies.¹² This procedure is suitable for defects resulting from chemicals, including war gases, acid vapors and hydrogen sulfide.

Phlyctenular Conjunctivitis

According to A. L. Prigozhina¹³ phlyctenules and fleeting nodules are manifestations of varying phases of local allergy, closely related to tuberculous allergy Inflammation and infiltration occur if the sensitivity is mild, and necrosis if the sensitivity is severe.

Pseudomembranous Conjunctivitis

Treatment—K. C. Swan and J. H. Allen¹⁴ report that they obtained successful results in 3 cases of streptococcic pseudomembranous conjunctivitis by the oral administration of small doses of *sulfanilamide*.

Horsehair Sutures

The use of horsehair sutures for closure of the wound after the insertion of a glass sphere in performing the Frost-Lang operation is recommended by P. J. Hay.¹⁵

CONTACT LENSES

Indications—The usefulness of contact lenses not only for cosmetic but also for optical and occupational purposes is stressed by F. A Williamson-Noble ¹⁶ Contact lenses are of assistance in cases of conical cornea, facets of the cornea, pemphigus, myopia, aniridia, and albinism as well as for individuals engaged in football, baseball, hunting or shooting and in occupations in which fogging by steam or rain may occur.

CORNEA

Lye Burns

Treatment — Y D. Kaplan¹⁷ concludes from his series of cases of experimental lye burns in rabbits that *profuse* irrigation with water is the best first-aid treatment in these cases

Gilding From Sanocrysine

A. Urrets Zavalia and R Obregon Oliva¹⁸ have noted chrysiasis (gilding) of the cornea during treatment of pulmonary tuberculosis with sanocrysine The gold appeared as crystals in and near Bowman's membrane and as reddish-brown particles not only in the interstitial tissue of the cornea but also in Descemet's membrane.

Filamentous Keratitis

A case of filamentous keratitis attributed to hypofunction of the ovaries is reported by L. K Krachmalnikov.¹⁹

Hurler's Syndrome

M. L. Berliner²⁰ describes 3 cases of opacity of the cornea as part of the picture of Hurler's syndrome. A large head, prominent frontal bones, wide clavicles, kyphosis, dwarfism, deformity of the limbs with shortening and thickening of the long bones, widely spaced and irregular teeth, large and protruding tongue, and enlargement of the liver and spleen characterize this syndrome. Histologic examination reveals infiltration of a lipinlike substance in the tissues of the cornea, liver, spleen, lymph nodes, and the anterior lobe of the pituitary gland. Hurler's syndrome differs from other members of the group of lipidoses (viz, amaurotic family idiocy (Tay - Sachs), Niemann - Pick, Hans Schuller-Christian, and Gaucher), not only by the organs involved in the storage of lipin but also by the chemical nature of the lipin Biomicroscopic examination reveals that the cornea, which appears milky, contains yellowish white deposits not only in the middle but also in the deeper layers of the cornea. Blood vessels are absent. Histologic section reveals that the lipin is deposited in the spindle-shaped interlamellar spaces

Various Lesions

Treatment — According to S. K Kentgens²¹ local and systemic use of vitamin A in the form of an ointment or solution of *cod-liver oil* is of assistance in the treatment of herpes, keratitis punctata, and marginal and catarrhal ulcers of the cornea.

Opacities

A series of cases, which demonstrates that transplantation of cornea taken from a cadaver has a more beneficial effect on corneal scars than transplantation of cornea taken from the living is reported by S. L. Velter.²² These transplants are effective even in cases of very old scars.

Trauma

Treatment — From an experimental study of the action of *insulin* on corneal wounds, C. Dejean and P. Artières²⁸ conclude that a daily injection of 10 to 15 units of insulin shortens the healing period 2 to 4 days. Dejean and Artières removed a superficial portion of the cornea with a trephine and observed the time necessary for regeneration of the cornea stained with methylene blue

Keratitis

Treatment—According to S. M. Edison,²⁴ ionization with zinc is of assistance in the absorption of infiltrates and scars resulting from interstitial keratitis.

Ulcer

According to A. J. Rhodes²⁵ the conjunctival flora of coal mine workers are potentially dangerous and in hypopyon ulcer the organisms already present in the conjunctival sac, are the source of infection.

Treatment—The use of sulfanila-mide in the treatment of corneal ulcers is recommended by J. H. Bailey and E. Saskin ²⁶. They administered sulfanilamide by mouth in 9 cases of severe involvement of the eye. Six of these were cases of corneal ulcer resulting from chemical burns or from trauma. Improvement occurred quickly. A patient of 154 lbs. (70 kg.) is usually given 15 grains (1 Gm.) of sulfanilamide every 4 hours during the first 24 hours and 75 grains (5 Gm.) during the next 24 hours.

DRUGS

Adrenalin Sensitivity

I. A. Sharkovskiy²⁷ reported that after the subconjunctival injection of 3 minims (0.19 cc.) of adrenalin during a cataract extraction a constitutional reaction developed and the operation had to be discontinued. On the next day, petechiae appeared over the abdomen and chest and dry gangrene of the skin on the back of the hands developed. Sharkovskiy points out that adrenalin should be used cautiously in elderly people.

Pontocaine

Several cases of eczema of the hands as a result of the use of pontocaine have been observed by S. Sander-Larsen.³²

N. Shimkin³³ also reports several cases of eczema of the eyelids after instillation of a solution of pontocaine. He himself developed a dermatitis of the hands. A patch test in these cases usually reveals the presence of sensitivity.

Iodine

The fact that swelling of the eyelids and of the conjunctiva frequently occurs after the administration of iodides, even in the absence of an iodide rash, is discussed by H. K. Goldberg ³⁸ He reports a case which was characterized not only by redness and severe edema of the eyelids and conjunctiva, but also by blebs, bullas and infiltration of the cornea, discoloration of the iris, synechiae, and hypopyon in both eyes. Rapid improvement resulted when administration of iodides was discontinued

Sulfanilamide

Method of Administration — The concentration of sulfanilamide in the aqueous and in the vitreous not only after instillation in the conjunctival sac but also after oral administration of the drug was determined by W. G. Mengel ⁸⁴ His study reveals that greater concentration of sulfanilamide in the ocular fluids is obtained by oral administration than by instillation in the conjunctival sac

Paraldehyde as an Anesthetic Agent

Paraldehyde is considered one of the safest narcotic drugs by E. S. Rowbotham.²⁸ For eye surgery it is administered by rectum in conjunction with instillation of a local anesthetic in the conjunctival sac.

Cycloplegics

Benzedrine—O. Baratta²⁹ points out that benzedrine (amphetamine) is a mydriatic which acts by stimulation of the sympathetic nerve endings. The mydriatic effect of homatropine or atropine is increased when combined with benzedrine. Benzedrine cannot dilate a pupil contracted by pilocarpine but pilocarpine can counteract the effect of benzedrine Baratta states that benzedrine has no effect on intraocular tension

Homatropine and Benzedrine-According to L. S. Powell³⁰ homatropine and benzedrine in combination produce complete cycloplegia for practical purposes of refraction in a high percentage of patients between the ages of 16 and 31 years. Moreover, instillation of a solution of ½ to 1 per cent eserine salicylate result in complete return of accommodation in one-half hour. The procedure suggested is as follows: 2 drops of 2 per cent solution of homatropine are instilled 5 minutes apart, followed by 2 drops of 1 per cent benzedrine sulfate 5 minutes apart Refraction is performed in 60 minutes

According to H F Sudranski,³¹ instillation in the conjunctival sac of a solution of 5 per cent homatropine hydrobromide, combined with a solution of 1 per cent benzedrine sulfate, produces complete cycloplegia and good mydriasis. Moreover, the cycloplegic effect is of shorter duration because a smaller amount of homatropine is employed.

EYE

Sunken Appearance of Artificial Eye

Surgical Treatment — An operation for the correction of the sunken appearance of an artificial eye has been devised by J. M. Wheeler. 35 A horizontal incision is made in the conjunctiva completely across the fundus of the socket and the conjunctiva is dissected from Tenon's capsule. Tenon's capsule is incised vertically cutting deep into the orbital tissues A special hollow-glass body in which 4 grooves have been made for the recti muscles is implanted into the muscle cone behind Tenon's capsule Terion's capsule is sutured with mattress sutures so as to cause overlapping of the flaps. The conjunctiva is closed with interrupted sutures A pressure dressing is applied for 1 week

Burns

Treatment — D. I Berezinskaya³⁶ concludes from an experimental study of the rôle of *paracentesis* in the treatment of chemical burns of the eye that repeated paracentesis is of assistance in alkali burns of the cornea provided that the conjunctiva has not been destroyed. If the conjunctiva is necrotic, paracentesis is useful only when performed in conjunction with transplantation of mucous membrane

Immediate transplantation of buccal mucous membrane in most cases of burns of the eye is recommended by R. Denig ³⁷ He states that even if the burns are situated some distance from the cornea, the capillaries of the limbus may be damaged so that interference with the nutrition of the cornea may result. After excision of the necrotic conjunctiva at the limbus, transplantation of mucous membrane assists in producing hyperemia and new capillaries

resulting in an increased supply of nutritive material to the corneal tissues.

Examination

Malingering—A device for the detection of malingering by means of a Snellen chart illuminated with red, green or vellow rays from a sodium lamp is described by A. Bakker.³⁹ The patient is directed to keep both eyes open and to read the letters on the chart when a green glass is placed before his seeing eve. The green light is turned on the Snellen chart so that he reads with his seeing eye. Then a red glass is placed over the seeing eye and the red illumination is directed at the chart. The patient then reads again with his good eye Finally, another red glass is placed before the good eye and the sodium lamp is used Rays emitted by this lamp are absorbed by the red glass in front of the patient's good eye so that the patient reads with his allegedly bad eye without being aware of it.

Chalcosis

Two cases of chalcosis of the eyeball resulting from penetration of a particle of copper into the eyeball are reported by G X Gorovaya and M K, Rapoport ⁴⁶ They also report another case in which chalcosis developed after an ointment containing copper was employed for the treatment of trachoma

Herpes Zoster

A case of herpes zoster ophthalmicus which developed three days after an acute infection of the throat is described by F R Goldberg ⁴¹ The condition was associated with iritis, keratitis and nodules of episcleritis Corneal sensitivity was reduced in the other eye

Ichthyosis

F. C Cordes and M J. Hogan⁴² report a case of ichthyosis of both eyes associated with generalized ichthyosis of

the skin. The right cornea presented a pannus and the conjunctiva of both eyes was thickened and red without the formation of papillae or follicles. Ichthyosis of the eye should be treated symptomatically.

Inflammations

Treatment—The use of subconjunctival injections of neoprontosil for the treatment of ocular infections is recommended by R. T. Paton. 43 After anesthesia of the conjunctiva is obtained with a solution of $\frac{1}{4}$ per cent pontocaine hydrochloride, 0.3 cc. of a solution of 2.5 per cent neoprontosil is injected in the upper or lower cul-de-sac. The dye constituent of neoprontosil usually absorbs within 2 days, and the injection is then repeated. Satisfactory results were obtained in several cases of iritis, scleritis and interstitial keratitis. He concludes that small doses of neoprontosil injected subconjunctivally are effective in cases of severe intraocular and extraocular infections and are well tolerated by the eye.

Syphilis

Treatment - C. Stroobants and C. Schepens⁴⁴ point out that the arsenical derivatives are not only either weak or strong spirillicides but also that they may cause arsenic poisoning. In cases under treatment, poisoning by arsenic rather than the syphilitic process itself seems to be responsible for complications such as loss of the field of vision and reduction of visual acuity One case under treatment developed bilateral optic If this complication should occur, treatment with arsenic must be discontinued and sodium hyposulfite must be administered intravenously and by mouth. Treatment of syphilitic lesions of the eye by arsenicals is recommended in spite of the possibility of complications which may result from arsenic poisoning

Tuberculosis

Treatment—Remele⁴⁵ obtained complete cures in 25 out of a series of 35 eyes in 23 patients which were affected with tuberculous iridocyclitis, sclerokeratitis, choroiditis, papillitis, and retrobulbar neuritis by means of the gold preparation, Solganal B oleosum.

EYEBALL

Exophthalmos

E. J. Wynkoop and L. Hadley⁵¹ report a case of Schuller-Christian disease in a child about 3 years of age. The exophthalmos was associated with classical bony defects in the skull and with diabetes insipidus *X-ray therapy* and *proper diet* resulted in improvement.

Treatment—According to D. Marine⁴⁷ exophthalmos resulting from thyroidectomy in rabbits can be cured by *gonadectomy* or by the administration of *thyroxin*.

Intraocular Foreign Body

Extraction—Technic—W. B. Lancaster⁴⁸ recommends his technic for extraction of intraocular foreign bodies. To prevent hemorrhage he makes the incision with a diathermy knife and to prevent detachment of the retina he surrounds the incision with punctures made with a diathermy needle.

Roentgenography — To facilitate roentgen-ray localization of intraocular foreign bodies, M. Bujadoux⁴⁹ suggests marking the anterior pole of the eye by means of subconjunctival injections of thick lipiodol at 12 and at 6 o'clock on the limbus.

Nystagmus in Intracranial Tumor

The presence of rotatory pendulum oscillations, identical with miner's nystagmus, in a case of tumor of the hypo-

physeal region in a man 40 years of age is reported by W. Friemann.⁵⁰ The patient complained of headache, vertigo and impairment of sight. The optic discs were pale and temporal hemianopsia was present. The roentgenogram revealed a widened sella turcica with atrophy of the dorsum, indicating a tumor of the hypophyseal region.

Irradiation was effective in restoring the vision and administration of **scopolamine** in arresting the nystagmus

Tumors

According to W. Susman,⁵² intraocular tumors are of 3 types, neurogenic tumors of the retina (neuro-epithelioma, polar spongioblastoma, neuroblastoma and neurocytoma); sarcomas of the choroid with choroidal differentiation, malignant choroidoma, and melanomas of the choroid. The presence of pigment merely indicates that the choroid has been disturbed by the growth. Melanomas are rare

Eyelash Dyes

Three cases of eye affections which resulted from the use of dyes for coloring the eyebrows and the eyelashes are reported by I. M. Makhlin.⁴⁰ Two cases were cured by *irradiation* with *Bucky's border rays*.

EYELIDS

Cancer

Treatment — H. E. Martin⁵³ states that cancer of the eyelids is particularly significant because impairment of vision may result not only from destruction of the eye by the growth but also from the destructive effect of the treatment employed to eradicate the neoplasm. Any tumor of the eyelid should be considered potentially cancerous and any chronic ulcer or any ulcerated tumor should be

diagnosed as cancerous. A pinkish translucent tumor, fixed in the skin, which presents telangiectasis, is suggestive of basal cell carcinoma.

Small lesions may be treated by *irradiation* or by excision; moderate-sized lesions by irradiation; and extensive tumors either by *radical excision* or by excision combined with irradiation.

Chancre, Primary

A case of primary chancre of the eyelids is reported by F. Csillag.⁵⁴ The lower eyelid became swollen, thickened and hard. A yellowish crust formed upon the surface but no ulceration appeared. The upper eyelid later developed a similar appearance, and the preauricular gland became enlarged. The Wassermann reaction was positive After administration of antisyphilitic treatment the lesions disappeared.

Elephantiasis

A case of Recklinghausen's neurofibromatosis associated with mental deficiency and endocrine disturbances in a farmer, 29 years of age, is described by IF W. Meyer. 55 The right upper eyelid had become thickened and increased in size so that it extended over the lower eyelid. Neurofibroma with elephantiasis of the eyelid was diagnosed after a histologic examination was made of several nodules in the skin of the left shoulder

Epithelioma

Treatment—A case of nonepidermoid epithelioma of the eyelid which after treatment by radium resulted in such damage to the eye that enucleation was necessary is reported by M. A. Dollfus, A. Hudelo and Paulin ⁵⁶ Histologic examination revealed degeneration and ulceration of the cornea, swelling of the lens with the formation of crystals and spherules, pigmentation of the retina,

thrombosis of the blood vessels in the iris and atrophy of the ciliary body.

Ptosis

Plastic Surgery — J. M. Wheeler⁵⁷ has devised an operation for the correction of ptosis by attachment of strips of orbicularis muscle to the superior rectus muscle. An incision 25 mm. long is made in the skin at the level of the upper border of the tarsus. The edges are undermined and a horizontal incision is made through the orbicularis muscle. 4 or 5 mm. above the edge of the tarsus and carried through the tarso-orbital fascia and the levator tendon. The dissection is carried through Tenon's capsule to the sclera on each side of the tendon of the superior rectus muscle. The superior rectus muscle is picked up on a squint hook. Two strips of orbicularis muscle, 4 mm. wide and 10 mm. long, one nasal, the other temporal, are dissected from the tarsus so that their free ends are directed toward the canthi while their medial portions remain attached to the tarsus The free ends are then attached to the upper surface of the superior rectus muscle with 000 chromic catgut sutures.

Transillumination

According to E. H. Wood⁵⁸ transillumination of the eyelid is of assistance in the study of chalazions, the lacrimal drainage apparatus, and injuries to the eyelid; for the detection of foreign bodies of the eyelids; and for differentiating between vernal catarrh and trachoma. In trachoma the follicles transilluminate clearly, while in vernal catarrh they produce dense shadows

Trichiasis

Surgical Treatment—For the surgical treatment of trichiasis, E. Klauber⁵⁹ advocates the use of a graft taken from

the bulbar conjunctiva instead of from the buccal mucous membrane.

FACIAL NERVE

Neuralgia

Treatment—C. Charlin⁶⁰ discusses 50 cases of essential neuralgia of the facial nerve. In 10 cases tuberculous lesions occurred at the site of the neuralgia and in 31 in the thorax. In 5 cases of the latter group, lesions were active clinically. Good results were obtained in 35 following administration of tuberculin.

GLAUCOMA

Blood Chemistry — According to H. Schmeltzer,⁶¹ quantitative investigation of the blood chemistry in 55 cases of primary glaucoma and in 45 cases used as controls revealed the presence of high cholesterol and high phenyl group values in 94 per cent of the cases. He is of the opinion that these findings are indicative of a hepatic disorder. Therefore, he recommends a low fat and low protein diet and the avoidance of alcohol, nicotine and caffeine in conjunction with the injection of small doses of insulin

Etiology — P. Weinstein⁶² believes that a relationship exists between glaucoma and the blood pressure. Moreover, in glaucomatous patients an endocrine dysfunction is present which exerts its effect through the circulatory system.

Glaucoma capsularis is discussed by A. Maghraby⁶³ who states that 8 per cent to 12 per cent of cases of glaucoma result from exfoliation of the capsule of the lens. This condition, which occurs in patients about 65 years of age, is characterized by heaviness and discomfort of the eyes associated with failing vision. The diminished visual acuity results from increased tension and from opacity of the lens. Biomicroscopy re-

veals the presence of bluish-white fluffy masses attached to the pupillary border of the iris and fine bluish-white scales on the anterior surface of the lens. Increased tension was found in 16 of the 19 cases reported. He considers tension of from 22 to 25 mm. Hg as high when associated with exfoliation of the capsule of the lens. He advocates performing a broad iridectomy. In spite of the reduction of tension, the vision usually continues to fail because opacification of the lens is present.

According to F. G. Ibrahim, 64 syphilis may be one of the predisposing causes of primary glaucoma. He found syphilis in 38 of 220 cases of glaucoma, and in only 19 of 142 cases of senile cataract

Unfavorable Influences—M. I. Zaionchkovskii⁶⁵ has found that increased humidity has an unfavorable effect on glaucoma, especially on acute inflammatory glaucoma. Barometric pressure does not affect glaucoma.

In some cases of glaucoma, according to H. I. Medvedev and L. B. Zats⁶⁶ retrobulbar injection of a solution of novocain and adrenalin results in elevation of the intraocular tension.

Treatment—Eleven cases of glaucoma simplex in which application of adrenalin tampons was effective in reducing the intraocular tension have been reported by Lottrup-Andersen ⁶⁸

According to R. P. Wilson, 69 intramuscular injections of cortin in cases of chronic primary glaucoma have no beneficial effect. Moreover, a slight increase in intraocular pressure resulted in 3 cases

According to Fantl,⁷⁰ Lindner's fistula operation is useful only as a preliminary procedure to reduce markedly increased intraocular tension or to increase the depth of a shallow or obliterated anterior chamber. The hypotony produced is usually only temporary. This conclusion is

based on his experience with Lindner's operation in 50 cases

Satisfactory results were obtained by A Bencini⁷¹ in 5 cases of chronic glaucoma by means of *Holth's iridencleisis operation*.

A modification of the Lagrange operation for simple glaucoma is recommended by J. M. Griscom.⁷² A conjunctival flap is dissected to the limbus. With a cornea-splitting knife, an incision 3 mm long is made in the superficial layers of the sclera 2 mm. above and parallel to the limbus. The point of a keratome is then introduced into this scleral incision and advanced over the anterior surface of the iris until the scleral incision is about 5 mm. wide. A scleral lip, 15 mm wide and 4 mm. long, is excised. A broad basal iridectomy is performed and the conjunctiva is sutured. In 90 per cent of his series of 50 cases, the intraocular tension was reduced to normal.

E Redslob⁷⁸ succeeded in reducing the tension in a series of eyes which had become blind as a result of chronic glaucoma by reducing the pH of the vitreous. This was accomplished by injecting 0.7 per cent phosphoric acid into the vitreous In some cases, 2 per cent phosphoric acid was injected. The tension usually decreased after 1 or 2 injections and pilocarpine then became more effective.

Filtration—To insure filtering scars in recent sclerectomies M. Sobhy Bey⁶⁷ advocates injections of milk or other foreign protein to prevent hypotony and instillation of atropine to increase the tension so that the aqueous will be forced through the scleral opening

IRIS

Boeck's Iritis

N. R. Blegvad⁷⁴ points out that Boeck's iritis may be either a nodular type or a

serous type, commonly associated with band-shaped keratitis.

The nodules in Boeck's iritis are usually large, irregular, reddish-yellow in color and are traversed by numerous fine blood vessels. Healing occurs without atrophy or scarring.

The nodules in tuberculous iritis are smooth, round or oval and dirty-white with a yellow tinge. They may penetrate the iris and become enveloped by blood vessels. Healing occurs with scarcely visible scars but at times atrophic areas form in the iris tissue.

LACRIMAL DUCT

Syphilis

A case of syphilis of the lacrimal duct which simulated acute dacryocystitis is reported by P Desvignes.⁷⁵ The diagnosis was confirmed serologically and therapeutically. Only 12 cases of acute syphilitic infection of the sac are reported in the literature

LACRIMAL GLAND

Tumors

Surgical Treatment — In cases of mixed tumor of the lacrimal gland, T. E. Sanders⁷⁶ recommends early and complete surgical removal, because irradiation is not effective. He reports 12 cases, 10 of which have been followed for more than 2 years. Out of 11 of these cases, in spite of surgical removal, recurrence took place in 10. One patient, who refused operation, died 6 years later as a result of local extension and metastases

LACRIMAL SAC

Dacryocystitis

Etiology—From his investigation of a series of 38 cases of dacryocystitis oc-

curring in patients between 1 and 15 years of age, K. O. Granstrom⁷⁷ concludes that in 9 of these cases untreated congenital stenosis of the nasolacrimal duct was the etiologic factor.

Dacryocystorhinectomy—A new surgical technic for the treatment of chronic dacryocystitis is recommended by E. Cornet. His procedure, dacryocystorhinectomy, is similar to that of Dupuy-Dutemps, but a larger window is cut in the nasal mucous membrane and a corresponding window in the side of the lacrimal sac. The edges of 1 window are then sutured with continuous catgut sutures to those of the other window so that an anastomosis is formed. The skin and the canthal ligament are sutured in the usual manner.

LENS

Anterior Capsule

Fourteen cases of semile exfoliation of the anterior capsule of the lens are reported by W. Wiederkehr.⁸¹ Vacuoles, which form in the anterior capsule of the lens, separate and loosen the lamellae of the capsule. These lamellae may be deposited on the posterior surfaces of the cornea and iris and on the pupillary margin. Obstruction of the angle of the anterior chamber may ensue. Five of these cases were associated with glaucoma.

CATARACT

Pathology—The pathology of complicated cataracts resulting from lesions within the eyeball, such as inflammations, glaucoma, tumors, necrosis of surrounding tissues, and from mechanical causes is discussed by B. Samuels.⁸² Samuels advocates postponing surgical interfer-

ence until at least 1 year after the eye has become free from inflammation. He recommends preliminary iridectomy and extracapsular extraction.

Etiology—Two cases of dinitrophenol cataract are reported by J. Sedan.⁸³

A. Winkler⁸⁴ discusses dermatogenous cataracts reported in the literature and describes 1 case in his own experience This occurred in a man, 27 years of age, who had had eczema since the age of 4. Nuclear and cortical opacities and characteristic anteropolar, shield-shaped subcapsular opacities were present in both lenses. Urinary examination revealed an abnormal protein metabolism

Extraction—To insure a permanent pupillary opening, P A. Chandler⁸⁵ advocates performing a preliminary inferior iridotomy in cases of cataract complicated by posterior synechiae or by a pupillary membrane After the usual corneal incision is made, the posterior synechiae are freed with a spatula, and with a pair of Noyes scissors the lower margin of the iris is incised toward its root

Intracapsular extraction with peripheral iridectomy using Arruga or Kalt forceps is recommended by G. F. Cosmetatos ⁸⁶ Thirty-eight per cent of his series of 585 cases of cataract were delivered without rupture of the capsule.

A sucking disc for intracapsular extraction of cataracts has been devised by T J Dimitry ⁸⁷ This instrument consists of a hollow needle 1 inch long, with an enlarged sucking disc 4 mm. in diameter on its distal end. The other end is attached to an accurately ground 2 cc glass syringe, the resisting power of which is 70 pounds of hydraulic pressure. The disc is applied to the lens with the spring plunger forced down. When the plunger is released, the lens adheres to the disc by suction. Vibration of the capsule or

pressure at various parts of the capsule may be obtained by gently pressing or releasing the plunger.

Intracapsular extraction is contraindicated in nuclear, intumescent, and hypermature cataracts but it is the method of choice in most cases, according to P. Bonnet and L. Paufique.⁸⁸ They advocate preliminary iridectomy in cases complicated by synechiae or by increased intraocular tension, and in some cases of diabetes.

Secondary Membrane-Van Lint89 describes his method of extraction of a secondary cataractous membrane. He advises making an incision and a counter incision at the limbus with a Graefe knife. The temporal incision is made about 2 to 3 mm long, while the nasal incision is made 5 to 6 mm in length. A cystotome is introduced into the anterior chamber through the small temporal incision so that it crosses the chamber and passes behind the nasal iris The blade is turned backward and drawn lightly through the capsule bringing it toward the center of the pupil A capsule forceps is introduced through the larger nasal incision and the edge of the capsule is grasped and extracted in its entirety by gentle rotary traction

Ectopia

Treatment—In cases of ectopia lentis, extraction by means of a loop in conjunction with a wide preliminary iridectomy is recommended by C C Clarke. He has found that discissions are usually unsatisfactory.

Lenticonus, Posterior

A case of posterior lenticonus in 1 eye of a man, 20 years of age, is reported by K Porsaa ⁹¹ Biomicroscopy revealed a symmetrically rounded bulging of the posterior capsule of the clear lens toward the vitreous; the other eye was normal.

MYOPIA

Heredity—P. A. Jaensch⁹² points out that heredity plays a definite rôle in the development of myopia. Moderate myopia (under 6 diopters) usually follows the dominant type of heredity, while high myopia and progressive myopia follow the recessive type.

From his investigation of the rôle of heredity in the refractive error of over 4000 patients belonging to 878 families, L. Paul⁹⁸ concludes that if both parents are emmetropic, only 10 per cent of the first generation are myopic. If one parent is myopic, 30 per cent of the offspring, and, if both parents are myopic, 60 per cent of the offspring are myopic. High myopia occurs more frequently in families in which the mothers are highly myopic than in families in which the mothers are emmetropic or mildly myopic.

OPHTHALMIA, GONORRHEAL

Treatment — From their experience with *sulfanilamide* in the treatment of gonorrheal ophthalmia, F A. Barbour and H. A Towsley⁹⁴ conclude that with this drug corneal complications occur less frequently and that the hospitalization period is reduced

They point out that although newborn infants require a larger quantity of sulfanilamide, it is well tolerated

OPTIC CHIASM

Arachnoiditis, Traumatic

Five cases of traumatic opticochiasmatic arachnoiditis are reported by C. Kenel ⁹⁵ In each case a severe frontal injury was followed by headache, insomna, dizziness, diminution of central vision, bilateral peripheral contraction of the fields, and increased pressure in the

retinal arteries. Four cases were operated on and a fibrous or fibrinous membrane was removed. Immediate improvement resulted but the symptoms recurred eventually. No operation was performed on the fifth patient.

OPTIC NERVE

Atrophy

According to K. I. Merkulov, 96 a posttraumatic optic atrophy is diagnostic of a fracture of the skull Such a fracture is usually located in the frontal region. Merkulov reports 52 cases of injury of the skull in which unilateral optic atrophy developed as a result of an injury in the region of the optic canal resulting in strangulation of the optic nerve and bleeding into its sheath

Treatment — Decortication of the common and internal carotid arteries for the treatment of atrophy of the optic nerve is advocated by B. Mamedov. This procedure is more effective in young persons than in adults and is ineffective in atrophy of the optic nerve resulting from syphilis. In atrophy associated with retinitis pigmentosa, this procedure should be supplemented by vitamin therapy.

In 4 cases of syphilitic atrophy of the optic nerve reported by A. I Vilenkina, 98 improvement was obtained by lowering the intraocular tension.

Glioma

Diagnosis—A case of primary glioma of the optic nerve is reported by C W Rand, R. Irvine and D. L. Reeves⁹⁹ in a boy, 4 years of age, who presented unilateral exophthalmos Intracranial exploration revealed enlargement of the optic nerve which on histologic examination proved to be a polar spongioblastoma. The eye was enucleated with the

remaining portion of the optic nerve. Glioma of the optic nerve is usually characterized by neuritis or atrophy of the optic nerve, progressive exophthalmos and roentgenographic evidence of enlargement of the optic foramen.

Optic Neuritis

A case of bilateral optic neuritis with transient blindness and meningoencephalitis which occurred in a child, 14 months of age, 14 days after vaccination is reported by H. Scheyhing. 100 Intramuscular injections of convalescent blood from a vaccinated person and daily lumbar puncture resulted in recovery Eighty-nine cases of postvaccinal encephalitis have been reported in the literature, 31 of these were fatal.

Papilledema

From a survey of ophthalmologic symptoms associated with intracranial tumors, F. Bush and H. U. Moller¹⁰¹ conclude that in cases of choked disc, the visual acuity is unaffected until secondary atrophy occurs Papilledema was present in 70 per cent of a series of 352 cases of intracranial tumor and it was greater on the side of the tumor in 25 per cent. The pupillary reactions were affected in 19 per cent and the ocular motility in 12 per cent of the cases. Hemianopsia was present in 25 per cent of 96 cases which presented defects in the visual fields.

Retrobulbar Neuritis

Lymphocytosis—O. Dymling¹⁰² reports that a study of the blood in a series of 27 cases of retrobulbar neuritis revealed a lymphocytosis with a normal or slightly increased white count. He believes that the lymphocytosis indicates a deficiency of vitamin B

Etiology—From a study of 189 cases of retrobulbar neuritis, P. Cibis¹⁰³ concludes that disseminated sclerosis was the probable cause in 40 per cent of all

cases, in 60 per cent of the acute cases and in about 70 per cent of the acute forms which remained after excluding all cases in which other causes were probable. No etiologic factor was proved in 55 cases.

OPTIC TRACT

Trauma

A case of permanent injury to the visual pathway in an aviator, who at an altitude of from 5000 to 6000 meters suddenly developed headache, vertigo, and blurring of vision, is reported by W. Lohlein. 104 Vertigo, nystagmus, right-sided hemianesthesia and hemianopsia persisted after he landed. The findings are attributed to rupture of a cerebral blood vessel in the visual pathway above the optic tract.

OXYCEPHALY

Surgical Treatment—J E J. King¹⁰⁵ describes his procedure for the surgical treatment of oxycephaly, a condition characterized by premature closure of the sutures of the skull resulting in an arrest of the growth of the brain, exophthalmos, papilledema, and optic atrophy. An 8-year-old boy was operated on in 2 stages, 1 side of the skull at a time. The operation consists of boring holes, 5 cm apart through the skull, and connecting these holes by linear cuts through the bone so that a mosaic of skull fragments is formed which lie on the dura Separation of the fragments permits the brain to expand.

RETINA

Angiopathy

Retinal angiopathy resulting from trauma is described by A. J. Bedell. 106

In these cases the fundus usually presents large, soft, white fluffy clouds anterior to the retina and many hemorrhages on the retina, on the exudate and parallel to the vessels. Three types of cases are reported; the fundus presented retinal angiopathy in a case of fracture of the lumbar vertebrae: in another case in which compression of the chest, traumatic asphyxia and fracture of the dorsal vertebrae occurred; and in a third case in which there was a history of direct injury to the head. In this case only the eye on the side of the injury was affected. In the first 2 cases, bilateral lesions were present. In all these cases, when pallor of the disk develops, progressive optic atrophy should be suspected.

Caliber of Arterioles

P L. Cusick and W. E. Herrell¹⁰⁷ report that in 5 patients who had an idiosyncrasy to tobacco, the caliber of the retinal arterioles was reduced after smoking. The same reaction occurred in 20 out of 25 patients undergoing the cold pressor test The reduction in caliber is attributed to increased vasomotor tonus rather than to active angiospasm and is accompanied by a rise in systemic blood pressure. They conclude that the generalized narrowing of the retinal arterioles in many cases of hypertension results from active vasoconstriction or increased vasomotor tonus rather than from actual structural changes in the walls of the vessels.

Detachment

Etiology—S. S. Kovarskaya and S. I Sorkına¹⁰⁸ reported 5 cases of detachment of the retina which they considered tuberculous The diagnosis of tuberculosis is based on the youthful age of the patients, the subretinal striae, the infiltrated foci in the fundus and the tortuosity of the vessels.

Retinitis, Central

Four cases of central retinitis resulting from looking at a solar eclipse are described by N. N. Makarov. 109 This type of scotoma of electric ophthalmia usually develops 6 to 8 hours after exposure.

Retinitis Pigmentosa

Treatment — Treatment of retinitis pigmentosa and of syphilitic optic atrophy by lowering the intraocular tension and simultaneously by elevating the blood pressure is recommended by I A. Vasserman. 110 By this procedure Vasserman obtained definite improvement in 6 out of a series of 11 cases of retinitis pigmentosa in from 2 to 7 months He instilled miotics to lower the tension and administered caffeine and strychnine to elevate the blood pressure Vision was improved in almost all cases Enlargement of the visual field occurred in only 3 cases

SCLERA

Plaques

Pathology — According to A. M. Culler, 111 plaques of the sclera usually occur in patients over 60 years of age These plaques which are degenerative rather than developmental in character do not produce symptoms

Sympathetic Ophthalmia

Treatment—Z. Okolow-Hyrnkiewiczowa¹¹² reports 3 cases of sympathetic ophthalmia in which favorable results were obtained by treatment with atropine, dionin, hot fomentations, intravenous administration of arthrosan (sodium phenyleinchonate and sodium salicylate), urotropin, autohemotherapy, and increasing doses of an antituberculosis antigen.

Trachoma

Treatment—P. Burnier⁸⁰ obtained a diminution in secretion, photophobia. lacrimation and blepharospasm in 30 cases of trachoma by the administration of sulfanilamide.

Lacrimal Sac—According to P. G. Kostenko and R. Z. Kopit,⁷⁹ no characteristic microscopic findings are present in lacrimal sacs extirpated from cases of trachomatous conjunctivitis. Their conclusion is based on the histologic examination of 33 extirpated lacrimal sacs, 9 of which were removed from cases of trachoma.

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OTORHINOLARYNGOLOGY

Edited by Francis L. Lederer, M.D.

LARYNGOLOGY AND DISEASES OF THE NECK

By Louis Zolo Fishman, M.S., M.D.

LARYNX

In Infancy and Childhood

The larynx of the infant is more accessible than that of the adult, because early in life it is at a high level in the neck (third or fourth cervical vertebra). Consequently, even in a struggling infant-if the mouth is opened by placing a finger between the upper and lower jaws, and the head is held gently —the larynx can be seen with a mirror which needs to be placed only behind the base of the tongue where the epiglottis immediately presents itself. In the adult, it is at the considerably lower level of the sixth cervical vertebra Heatly¹ calls attention to a significant number of diseases of the larynx in infancy which are not only identified with this age-period by virtue of their congenital origin but also by their dependence upon well-defined morphologic characteristics associated with the development of this organ: The angulation of the glottis and the narrowness of the subglottis indicate at once, and this is substantiated clinically, that an otherwise benign, inflammatory process of the larynx is a serious menace when it occurs in the infant Obstruction of the larynx can be so suddenly complete as to lead to death by asphyxia This mishap can be avoided by early and repeated inspections in all cases of laryngeal disturbances; treatment can then be both opportune and adequate

In a series of 20 cases reported by Heatly the following diseases and their incidence were found to exist:

	Nur	nber of
Final Diagnosis	(Cases
Congenital laryngeal stridor		12
Paralysis of the vocal cord		2
Tumor of the larynx .		1
Congenital web		1
Subglottic tumor		1
Subglottic stenosis		1
Tumor of the mediastinum		1
Congenital anomaly of the ligamento	ous	
attachments of the sternum(?)		1
		<i>2</i> 0

It is not feasible to discuss here the treatment, which is more or less specialistic, of each of these conditions. Rather, attention is directed to the safety and ease with which the infant's larynx can be examined—usually without anesthesia

Tuberculosis—A review of statistics by Rubin and Galburt² shows that this is supposedly an uncommon disease in childhood. For example, of 500 tuberculous larynges examined by Mackenzie in 1882, only 1 was that of a child. On the other hand, of 100 children examined by these authors, 45 showed evidence of laryngeal pathology, of which 30 had tubercule bacilli in the sputum, feces or gastric contents. Although the most severe symptoms, aphonia and dysphagia, encountered commonly in adults, were also present in a few in this group of children, Rubin and Gal-

(451)

burt confirm observations made by previous workers that laryngeal symptoms are generally absent. They correspond very much with those which are known to occur in tuberculosis of the larynx in adults.

The principles in the treatment of tuberculous laryngitis in children are practically the same as for the adult. These have been covered in detail in past service volumes to which the reader is referred. Briefly, they consist of adequate constitutional and pulmonary management, collapse therapy of the lung when indicated and treatment of the larynx locally. The latter must be governed by the stage and extent of the laryngeal pathology, by the anatomical site, and by factors concerned with preserving the functions of this organ (respiration and phonation).

Hypnosis and Disorders of Voice and Speech

There is a great number of derangements of the mechanism of speech - sound-production (phonation) sound-transformation (articulation) which are unquestionably due to some one or more types of neurosis Today, the etiologic factors involved in these cases are no longer fantasies of the physician, but are recognized as established facts. The indecision manifest in a great array of literature revolves around the selection of method or methods by which a psychosomatic disease should be treated. This state is nevertheless a favorable indication of progress when compared with the recent past when "shock therapy" was commonly performed in such patients; if a first success was only short-lived, the patient was blamed, rather than the medical practice There is little need to repeat the fact that the etiologic factors of neurosis are as real as though some

well known bacterial agent were concerned. Hypnosis has been advocated as a type of empirical but lasting form of therapy in cases of neuroses. Such a method has been successful in a number of cases of voice and speech disorders treated by Levbarg.3 The following types are reported in his series. (1) Dysphemia clonica; (2) phobia of speaking before strangers; (3) diplophonia (amblyphonia); (4) falsetto voice; (5) spastic tonic aphemia; (6) spastic speech. It is generally considered, however, that hypnosis is a shortcut rather than an adequate solution of the psychical conflicts which become translated into somatic dysfunctions. In selected cases, this form of therapy, as well as elementary forms of psychoanalysis, merits the consideration of the laryngologist, who, as indicated by Levbarg, can acquire the technic

Spasm of the Larynx and So-called Tracheal Collapse

Cole⁴ recalls the attention of the general surgeon to a fact which has been of significance to the laryngologist, namely, the reactivity of the larynx reflexly to local and/or to remote stimuli number of cases of respiratory obstruction was encountered during thyroidectomies. This event has been explained by many on the basis of collapse of the trachea following the removal of the thyroid gland It should be remembered, as Cole demonstrates by his experiments, that most of these are not due to tracheal collapse, which occurs when the tracheal cartilages have been destroyed (chondromalacia), but are rather the result of a contraction of the circular muscles of the trachea, and, in most cases, of the adductors of the larynx (glottic spasm). Treatment is obviously based on the nature of the obstruction, which can be determined by

inspecting the larynx. The diagnosis which attends such an inspection is of paramount importance and can be accomplished quickly, to the immediate relief of all concerned, when, as is usual, a spasm of the glottis is found to exist. The latter can then be relieved by increasing the depth of narcosis.

Paralysis of the Larynx

A new operation for restoring the patency of the lumen of the larynx in cases of bilateral, "so-called" abductor, vocal cord paralysis has been devised by King.⁵ It consists mainly of another type of plastic procedure in which only the inner and posterior surfaces of the anterior belly of the omohyoid muscle are dissected free; it is then cut away from the hyoid bone and sutured to the dorsal aspect of a properly prepared arytenoid cartilage. To shorten the muscle to the desired length, its belly is ligated 3/4 inch below the hyoid bone and its distal portion divided. An evaluation of this procedure is difficult, particularly in the absence of actual experience with it. However, the anatomic and physiologic principles involved, the description of the operation and the results following it suggest quite a number of conflicting ideas. King reports 3 cases In 2, the glottis is described as having been widened only moderately so that there is clinical improvement in so far as the ability to perform moderate physical duties; in the third case, there was no improvement at the time when the report was submitted for publication

Acute Laryngo-Tracheo-Bronchitis

Evans⁶ reports 3 cases of this disease One due to hemolytic streptococcus, the other 2, to *Staphylococcus albus* He found that the formation of crusts and plugs within the tracheobronchial tree and the occurrence of abscesses were

characteristic of staphylococcic infections, whereas, in the streptococcus infections, edema, marked toxicity and dehydration predominated. After other therapy had failed, the use of staphylococcus bacteriophage employed in the form of instillations through a tracheotomy into the tracheobronchial tree and then followed by aspiration of the crusts, resulted in rapid improvement and finally in cure He does not indicate the use of one of the sulfanilamide preparations, but remarks that early tracheotomy, use of a steam tent and of measures to overcome dehydration and toxicity are sufficient to obtain a recovery His conclusions are:

- "1. The proper handling of these cases requires that they should be recognized early for what they are, and that valuable time should not be lost in treating them with antitoxin.
- "2 Immediately upon suspicion of the diagnosis the patient should be transferred to a hospital where direct laryngoscopy and bronchoscopy should be carried out at once and where more active treatment such as tracheotomy may be done at a moment's notice.
- "3. If time permits, prior to operation, roentgen study should be made; otherwise it should immediately follow the tracheotomy.
- "4. Other essentials in the treatment of these cases are:
 - "a Constant competent special nursing care.
- "b A comparatively small-sized room in which the air can easily be kept well saturated, at all times, with steam containing tincture of benzoin.
- "c. A room equipped with a properly functioning suction apparatus
- "d. Forcing fluids either by mouth, rectum or by clysis, especially in streptococcus cases.
- "e In the staphylococcus cases, staphylococcus bacteriophage should be instilled into the trachea at frequent intervals, to be followed by immediate suction. Its use is urged in all such cases."

Pneumopericardium and Pneumomediastinum

The extravasation of air from the lung into the extrapulmonary regions in cases of obstructive lesions of the

larynx or of the tracheobronchial tree is an incident rather than a complication and its appearance may assume alarming proportions. Graebner⁷ reviews the literature and reports a series of cases from which he concludes the following:

- "1. Pneumopericardium and pneumomediastinum may occur at any time in the course of acute obstructive laryngitis. Their occurrence is directly influenced by obstruction of the upper and lower part of the respiratory tract
- "2. The complication is not directly due to, or proximately the result of, tracheotomy per se It occurred in a case in which tracheotomy was not performed; it was apparently present prior to operation in aother, and sealing the tracheotomy wound against air in 3 cases did not prevent its occurrence 24 to 48 hours later
- "3. The conditions do not play a conspicuous part or influence the course or prognosis of the disease with which they are associated
- "4. Pneumopericardium and pneumomediastinum are of relatively frequent occurrence Repeated roentgen and physical examinations at short intervals will probably reveal positive examples that may easily be overlooked
- "5 The mode of production of spontaneous pneumopericardium is unknown"

Abscess of Larynx

In localizing types of abscesses of the larvnx, Woodson⁸ discusses the etiology and diagnosis upon which treatment is based Indirect larvingoscopy will disclose in some cases the location of the abscess; in other cases, the larvnx will be found to be diffusely edematous Tracheotomy is performed when the obstruction interferes with breathing. When the abscess is localized it can be opened by incising it from within and aspirating through the larvingoscope whatever purulent secretions present themselves Extralaryngeal surgery is a procedure of choice when doubt exists concerning the exact site of the abscess, or when it is diffuse The extension of an infection from the soft tissue into one of the cartilages of the larynx, particularly into

TABLE 1
Histological Classification of Benign
Tumors of the Larynx

	Number	Per- centage
Neoplasms (329, or 45.6 per cent) Tumors of epithelial origin Adenomas Papillomas Tumors of connective tissue origin Fibromas Neurofibromas Fibrolipomas Chondromas and osteochondromas Angiomas Myxomas Cysts On-neoplastic tumors (393, or 54 4 per cent) Inflammatory tumors Xanthomas Amyloid tumors Epithelial hyperplasia and	1 194 6 1 1 7 26 58 35 332 4 18	
leukoplakia Prolapse of the ventricle	6	08
Totapse of the ventile		
Total	722	99 9

(New and Erich Arch. Otolaryng)

a hyaline cartilage (cricoid), may lead to permanent collapse of the lumen of the larynx Constitutional treatment in each case should be individualized and conducted by the internist or general practitioner in conjunction with the local treatment by the laryngologist

Benign Tumors

During a period of 30 years at The Mayo Clinic, 722 cases of benign growths of the larynx were seen; this is compared to 1100 malignant tumors of the larynx observed during the same period. Because of the difficulties which arise in any attempt to classify tumors, whether it be clinical or pathological in viewpoint, New and Erich⁹ include inflammatory new growths in the series of 722 cases (see Table I)

This table deserves study because it illustrates the great variety of benign

tumors which arise from the larynx. The 2 most frequent types of benign lesions were papillomas and inflammatory tumors. In the etiology of most

occur 10 times more frequently on the vocal cords than on all other parts of the larynx; 30 times more frequently on the true than on the false cords.

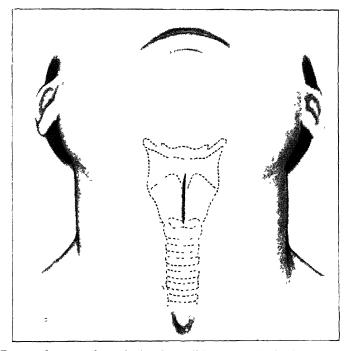


Fig 1-Incision through the skin (Myerson Arch Otolaryng)

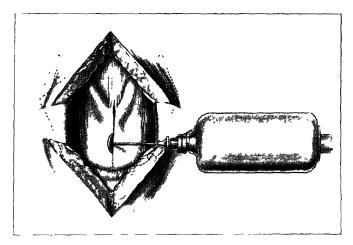


Fig 2—Rotary saw powered by a hand motor cutting through the thyroid cartilage (Myerson Arch Otolaryng)

of the 722 cases stated above, inflammation is given the greatest credence Excluding multiple papillomas which involve the larynx diffusely, the true cord is the site predilection: Benign tumors

There are no symptoms which may be said to be characteristic or diagnostic generally of such tumors. Many of these are discovered only on routine indirect laryngoscopy.

When symptoms are present, hoarseness is the most constant one, and the most serious symptom is obviously that of obstruction to breathing. The treatment of these tumors is to remove them by whatever method the particular case demands. Small tumors can be removed completely with a *punch forceps* by

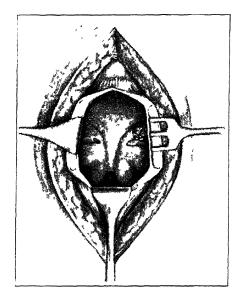


Fig 3—Retraction and Exposure (Myerson Arch Otolaryng)

indirect laryngoscopy, larger tumors are best approached by direct laryngoscopy using surgical diathermy. Suspension laryngoscopy is recommended in the removal of extensive lesions of the larvnx The latter method permits the surgeon to use both of his hands whereby actual surgical manipulations can be performed perorally, in many instances obviating the need of approaching the glottis from without (thyrotomy or laryngofissure) New and Erich caution against making a purely clinical diagnosis of a benign tumor of the larynx; not infrequently, these growths are found to be highly malignant neoplasms when studied microscopically Even benign tumors of the larynx should be thoroughly investigated for cellular signs of malignancy.

Carcinoma

Epiglottis—The surgical treatment of extrinsic carcinoma of the larynx, as reviewed in the supplement last year, is being reported more favorably each year It seems that the results of many years of experience are now being published in an attempt to revise a considerable number of orthodox and antiquated advices in therapy, and in answer to some of the vexing problems which these cases present. Carcinoma of the epiglottis has been and is still included by many among the inoperable or extrinsic types of malignancies of the larynx. It is gratifying to note that Tucker¹⁰ extirpated, by a thyrotomy, an epiglottis which was involved at its base by a carcinoma This patient is well after a 5-year period and has retained the normal function of his larynx. A second case is reported of a similar lesion in which a more adequate approach to the epiglottis was obtained by extending the thyrotomy wound upward and through the middle of the hyoid bone (preliminary tracheotomy, 2 weeks in advance) This second patient had an uneventful recovery as in most instances of other operative procedures on the larynx. Feeding was given postoperatively through a nasal catheter over a period of a week or 2-in the latter case, for 2 weeks. In both, the loss of the epiglottis did not interfere in any way with the production of sound. nor did it result in aspiration of food into the trachea—the true and false cords and the arveniglottic folds, rather than the epiglottis, prevent such an abnormal relay of the food

Intrinsic Carcinoma of the Larynx
—Negus¹¹ portrays graphically the difficulties which are encountered in the diagnosis of certain lesions of the larynx that may at one time or another simulate one another, or thought by some to pass from one type to another (chronic inflammatory process to one of malignancy). He has numerous illustrations which demonstrate the coexistence of different pathologic processes such as syphilis and carcinoma, tuberculosis and carcinoma, hyperkeratosis and carcinoma

In his last series of pictures it is of interest to note that a carcinoma of the larynx appeared on the cord opposite

proaches the problem in the following orderly and systematic manner:

- (1) A careful complete case history.
- (2) Indirect mirror laryngoscopy.
- (3) Complete general physical examination, particularly of the upper respiratory tract.
- (4) Roentgenologic studies of the sinuses, chest and neck.
- (5) Blood examination, both microscopic and serologic.

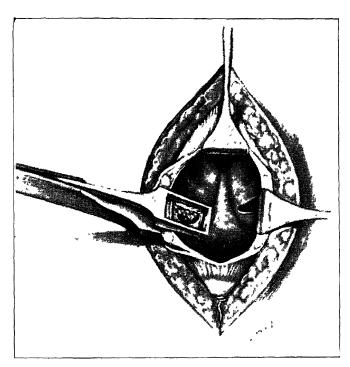


Fig 4—Removal of the cancer-bearing area and the cartilage in 1 piece by means of the special punch. (Myerson. Arch Otolaryng)

to the one which had been removed previously by laryngofissure. Negus warns against the possible mistake of labelling a benign tumor as malignant. We are always accustomed to warning against overlooking malignancies; in the above series of cases, malignancies were diagnosed in cases of simple papillomas and tuberculosis, an error of as great a magnitude as in the former instances.

Diagnosis of Laryngeal Malignancy—In the early diagnosis of carcinoma of the larynx, Lederer¹² ap-

- (6) Repeated examination of sputum
- (7) Direct laryngoscopy, bronchoscopy and esophagoscopy
 - (8) Biopsy

Treatment — From his experience with the treatment of intrinsic carcinomas of the larynx, he concludes that laryngectomy still offers the patient the greatest insurance against recurrence and for life. He advocates a 1-stage procedure, in which the larynx is removed without cutting through the muscles of the neck; only those muscles

which are attached to the thyroid and cricoid cartilages are dissected away: By "skeletonizing the larynx," a maximum amount of soft tissue is retained to lessen the deformity of the neck and to strengthen the anterior wall of the reconstructed pharynx; this assists in the prevention of a pharyngeal fistula. In the rehabilitation of the patient's voice, and therefore, in the readjustment of the patient to his environment, Lederer has found the Artificial Larynx to be of mestimable value both in its simplicity of construction and manipulation and in the short period of training required of the patient to resume his conversational contacts.

Laryngofissure-There are a number of clinics which advocate the practice for these cases, instead of laryngectomy, of only a resection of the affected vocal cord by laryngofissure. It is well to emphasize this marked difference in therapy which exists. Myerson describes the technic of the "so-called" laryngofissure, which is in truth a thyrotomy. This operation is indicated by Myerson13 to remove a strictly-limited intrinsic carcinoma of the larvnx. He does not advocate general anesthesia but uses instead phenobarbital for preliminary sedation, giving the patient 1 grain the evening before, 1 grain 6 hours before, and 3 grains 1 hour before the operation (it would seem that 3 times this dose would be more adequate) The larvnx is anesthetized with topical applications as in a laryngoscopy, and the neck, though not stated, is probably infiltrated with some such preparation as novocam

It should be indicated here, with respect to the removal of the thyroid cartilage, that, if the cartilage has been involved by the tumor, the case is far advanced and the operation is certainly not indicated by the definition of Myer-

son; in the type of case for which this operation is adopted by Myerson, it would seem to be unnecessary and even dangerous to remove an effective barrier, presented by the cartilage, against extension. Further, an incision beyond the laryngeal box might facilitate, by exposing the soft tissues of the neck, the extension of a malignant process otherwise confined within the larynx proper

NECK

Deep Infections of the Neck

Briefly stated, deep infections of the neck are most commonly secondary to inflammatory processes of the upper respiratory and gustatory tracts. Of these, the tonsils and teeth are most frequently portals of entry; the temporal (mastoiditis and petrositis) and sphenoid bones, less frequently. cause there exist today confusing concepts of the clinical entity described by Ludwig in 1836, known as Ludwig's Angina, Grodinsky's^{14, 15, 16} identification of it is of practical value: He limits the term to an "infection starting in the floor of the mouth, usually from carious lower molar or bicuspid teeth, spreading to the submental and submaxillary triangles (submandibular space) by fascial planes, and causing serious symptoms from edema of the tongue and glottis, mediastinitis, or toxemia. This definition automatically rules out spread by lymphatics, though obviously a periadenitis may lead to secondary fascial plane infection. It also practically elimmates the throat, tonsils, and pharynx as the seat of the initial lesion Infections in these structures spread by lymphatics, or from retropharyngeal or lateral pharyngeal abscesses, which in turn spread secondarily to the submandibular space and resemble Ludwig's angina in

the later stages.¹⁴" He states further that the degree of danger in infections of the head and neck is "dependent upon the location of the portal of entry, the degree of walling off by the inflammatory reaction, and the extent of spread before drainage is instituted. The im-

and alar fasciae (space 3) or the space between the alar and prevertebral fasciae (space 4).

"Infection in the visceral space is apt to remain localized at the site of origin. Infection in Space 3 may remain localized at the site of origin, but may

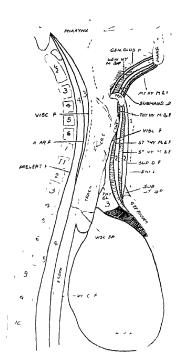


Fig 5—Diagrammatic drawing of fasciae of head and neck in midsagittal section (Grodinsky Ann Surg)

portance of a knowledge of the fasciae and fascial spaces in anticipating the routes of spread of infections and in planning proper incisions for drainage is obvious 15"

Regarding retropharyngeal and lateral pharyngeal abscesses, Grodinsky concludes that they occur most commonly in children under the age of 3, and are usually lymphogenous except when implanted directly by trauma. Also that "acute retropharyngeal abscess may involve the space between the pharyngeal wall and the visceral fascia (visceral space), the space between the visceral

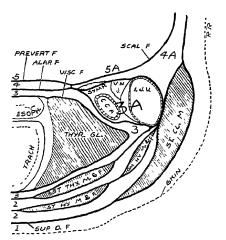


Fig 6—Diagrammatic drawing of tasciae of neck Transverse section approximately at the level of the sixth cervical vertebrae (Grodinsky Ann Surg)

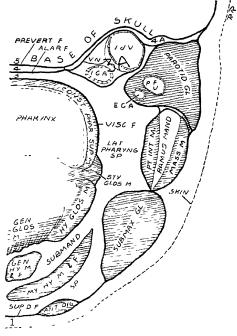


Fig 7—Diagrammatic drawing of fasciae of the head and neck. Oblique anteroposterior section showing the relation of the submandibular space to the lateral pharyngeal space and Spaces 3 and 4 (Grodinsky Ann Surg.)

also spread inferiorly and laterally through the neck to the superior mediastinum. It may also break through the alar fascia and reach Space 4. Infection

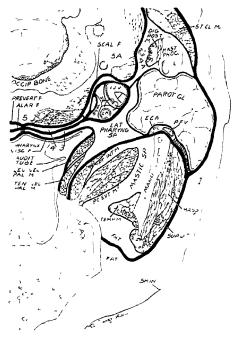


Fig 8—Transverse section of adult cadaver at level of hard palate Superior view (Grodinsky Ann Surg)

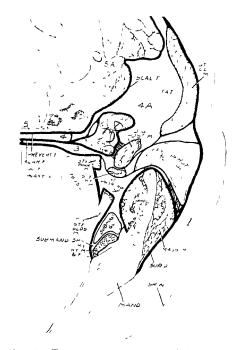


Fig 9—Transverse section of adult cadaver through the tongue and the palatine tonsil Superior view (Grodinsky Ann Surg.)

in Space 4 ('danger space') is apt to gravitate through the neck into the posterior mediastinum.

"The lateral pharyngeal space is directly continuous with Space 3 It may be primarily infected from the lateral pharyngeal wall or may be secondarily infected from Space 3, the parotid space, masticator space or submandibular space,

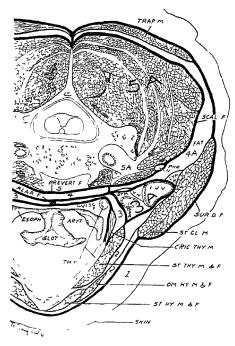


Fig 10—Transverse section of adult cadaver at the level of the thyroid cartilage Superior view (Grodinsky Ann Surg)

lice versa, primary infection within the lateral pharyingeal space may spread secondarily into those spaces. Infection in the lateral pharyingeal space extending into the submandibular space may resemble Ludwig's angina in the later stages

"Chronic retropharyngeal abscess is practically due to tuberculous caries of the cervical vertebrae. It is usually confined to Space 5 behind the prevertebral fascia, and usually gravitates to lower levels along the muscles taking origin from the vertebral column (psoas abscess). It may, however, remain local-

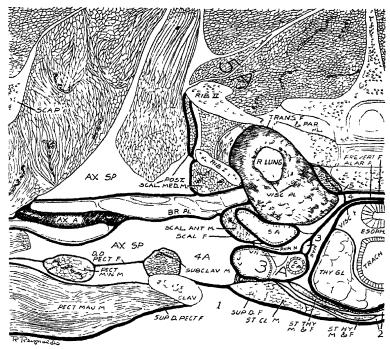


Fig 11—Transverse section of adult cadaver through the root of the neck Superior view (Grodinsky Ann. Surg)

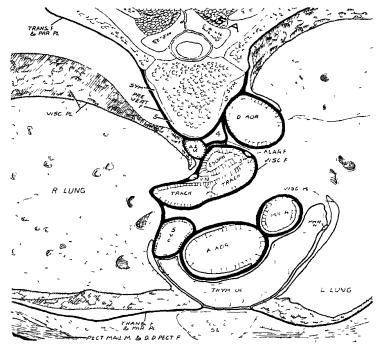


Fig 12—Transverse section of adult cadaver through the superior mediastinum Superior view (Grodinsky Ann Surg.)

ized in the cervical region, in which case it may rupture through the alar fascia and enter 'danger space' 4. It is commoner in adults.

"The clinical picture of pain, difficulty in swallowing and speaking, chills and fever, internal bulging of the pharyngeal wall, and external swelling of the neck should make early diagnosis possible.

"The treatment is chiefly surgical—early and adequate drainage. This

vertebra, may be effectively drained by cervical incision anterior to the sternocleidomastoid muscle (collar mediastinotomy). Collections in the posterior mediastinum below the level of the fourth thoracic vertebra demand posterior thoracic drainage (dorsal mediastinotomy).¹⁶"

Ligation of the Carotid Artery

A review of this chapter in Medicine is a natural sequence to the above. The

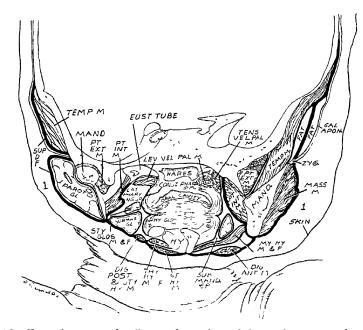


Fig. 13—Frontal section of tull-term fetus through base of tongue and posterior nares. Anterior view. (Grodinsky: Ann. Surg.)

may be internal through the mouth for cases confined to the posterior pharyngeal region (visceral space and Space 3) External incision is necessary for collections in the lateral pharyngeal space or inferior extensions in Spaces 3 or 4.

"The 'T' incision of Mosher with reflection of the submaxillary salivary gland is especially applicable for collections in the lateral pharyngeal space Spaces 3 and 4, including collections in the superior mediastinum and posterior mediastinum above the fourth thoracic

merits of ligation, especially of the common carotid artery or of one of the large trunks, have long been questioned. The most serious cases of hemorrhage from head or neck are those in which the internal carotid artery becomes eroded by an infectious process of the parapharynx. The surgeon has a tragic decision to make between not ligating this vessel and losing a life by exsanguination, or doing so with the knowledge that he may cause cerebral damage and death thereby An illustration of the seriousness of this procedure is seen in

the report by Fetterman and Pritchard¹⁷ of a case in which nasal hemorrhage of unknown cases persisted, despite local treatment and blood transfusions, until the red-cell count had fallen to 1,300,000. At this time, both the left external and internal carotid arteries on the side of the hemorrhage were ligated. Two and one-half hours mon ailments as: Headaches; neuralgia, epilepsy, and aortic aneurism. "This operation gained popularity up to the present century despite the fact that it was questioned by the more conservative surgeons. At present, though the procedure is much less common, and the indications for its use more limited, and despite the improvement in surgical

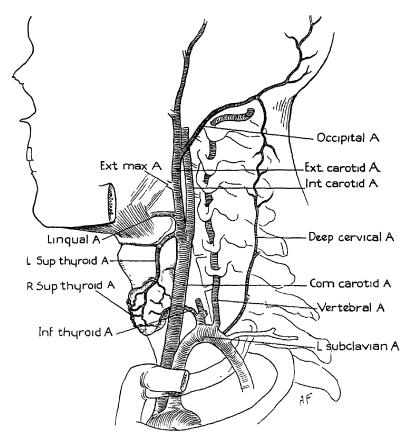


Fig 14—Showing the extracranial collateral circulation (Watson and Silverstone Ann, Surg)

after this the patient developed a rightsided flaccid hemiplegia and difficulty in speech and in swallowing. The patient remained an invalid for about 2 years until he finally succumbed to a disorder which was independent of the major neurologic disturbance.

It is of interest to note the variety of diseases and accidents for which this operation was undertaken in the past, among which were included such comtechnic, the operation, as Dr. Wood foresaw, continues to be a serious one which requires grave consideration before its execution ¹⁸"

Many of us have forgotten that there are marked and frequent abnormalities occurring in the main arteries of the neck and base of the brain—that the usual textbook description had already been found by Wendell in 1888, in a series of 200 autopsies, to be present in

only 38 per cent. To avoid cerebral damage, procedures have been devised to occlude slowly the common carotid artery; the Crile clamp has served such purposes. That this concept is faulty has

cancer, ligation of the common carotid artery as an emergency procedure is hazardous. The operative mortality in our series of 20 cases was 55 per cent Frequent variations and abnormalities

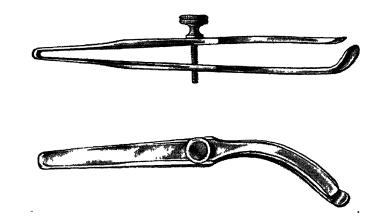


Fig 15—Clamp devised by Crile for gradual occlusion of the common carotid artery (Watson and Silverstone Ann Surg)

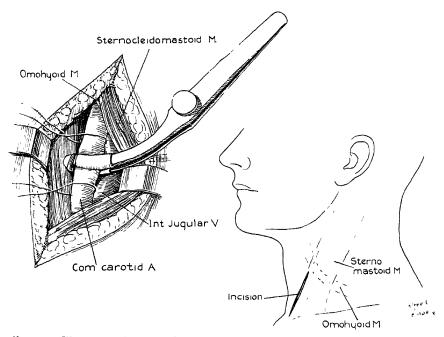


Fig. 16—Illustrating ligation of the common carotid artery using the Cille clamp (Watson and Silverstone Ann Surg.)

been proven by our own experience, the story of ligation is exposed and condemned by the unavoidable and unpredictable sequelae

They conclude "(1) These facts seem to indicate that in a patient with

in the anatomy of the arteries of the neck and brain suggest that these gross anatomic anomalies may largely explain the variety of cerebral complications occurring after common carotidartery ligation.

- "(2) Collateral circulation outside the cranium is probably of little significance after common carotid artery ligation.
- "(3) The use of the Crile clamp for gradual occlusion of the common carotid

patients who recovered were over 50 years of age.

"(5) The most frequent cause of death (70 per cent) was a brain complication, while embolus, hemorrhage, and edema

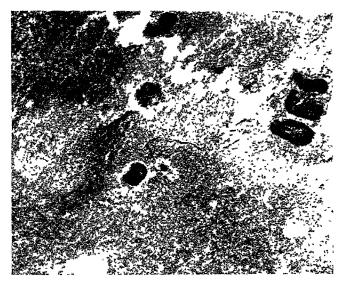


Fig 17—Microscopic paraffin section of centrifuged pus, and stained with hematoxylin and eosin (Randall Journal-Lancet)

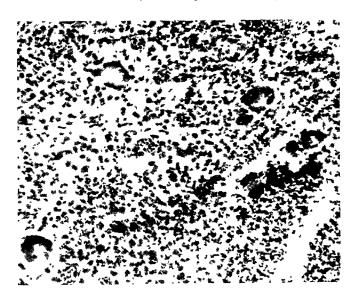


Fig. 18—Actinomycotic granulation tissue with numerous multinucleated giant cells (Randall Journal-Lancet)

artery does not improve the prognosis "(4) Age is apparently not a significant factor in prognosis. The 5 youngest patients in this series died postoperatively. Six of the 9 (66 per cent)

of the glottis are frequent factors in a fatal termination Postligation thrombosis probably occurs quite frequently.

"(6) Uncontrolled cancer, sepsis, debilitation, hemorrhage dehydration and low blood pressure are factors influencing a fatal outcome following ligation of the common carotid artery, but the pre-existing congenital blood vascular supply to the brain is an important of adrenalin to the first ounce, is injected in the skin for a distance of 4 cm. along the anterior border of the lower third of the sternomastoid muscle. The platysma is incised, the sterno-

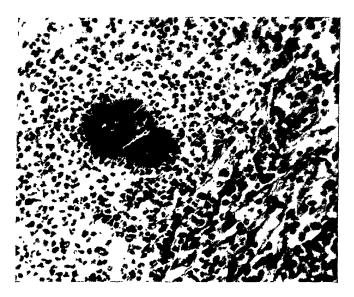


Fig 19—A young colony and early granulation tissue reaction showing the characteristic zones (Randall. Journal-Lancet)



Fig 20—Actinomycosis of the spleen Note detached mycelial filaments surrounded by wandering cells (Randall, Journal-Lancet)

factor, determining whether life can be maintained after 1 common carotid artery has been ligated."

"Operative Procedure—A 1 per cent novocain solution, containing 10 drops

mastoid muscle retracted laterally, and the common carotid artery located just below the crossing of the omohyoid muscle. The carotid sheath is incised and separated from the artery for a distance

of 1 cm.; then the Crile clamp is placed about the artery and 2, untied, No. 2 chromic catgut sutures placed around

a period of 24 hours. At the end of this time the packing is removed, ligatures tied and the clamp removed. If



Fig 21-Actinomycosis of the neck in a girl aged 13 (Randall Journal-Lancet.)



Fig. 22-Rapid extension of the actinomycotic process during inadequate treatment (Randall. Journal-Lancet)

clamp. The wound is packed open and gradual closing of the clamp, its jaws

the artery, 1 above and 1 below the cerebral symptoms develop during the the clamp slowly screwed shut over can be reopened and the flow of the blood re-established. One case in the series developed cerebral signs at the end of 6 hours. The clamp was unscrewed, but the patient became cyanotic and died. To be avoided in this procedure are such accidents as pressure necrosis of the artery walls, wound

ter are merely supportive measures and are secondary to surgical excision. Otherwise, the extension into contiguous tissue will tend to make the case more aggravated than if these measures were instituted vigorously at the very beginning



Fig 23—Actinomycosis of the head and neck of 2 years' duration, (Randall Journal-Lancet)

infection, hemorrhage and vagus and sympathetic nerve damage."

Actinomycosis of the Head and Neck

It is essential, according to Randall, ¹⁹ that material which has been aspirated from a chronic inflammatory mass should be studied, both by smear and by stained sections, for the characteristic colonies of actinomy cosis. Later in the course of the disease when sinuses are formed, the characteristic granules (sulfur bodnes) may not be so readily discovered. The cervicofacial region is most often affected, comprising, in the experience of Randall, 60 per cent of the cases. Treatment, after diagnosis has been made, is surgical excision, followed by radiation and potassium iodide: The lat-



Fig 24—One year after radical excision of the actinomycotic process $N_{\rm O}$ recurrence (Randall Journal-Lancet)

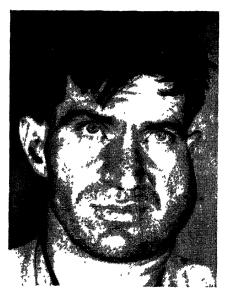


Fig 25—Actinonycosis of the parotid masseter region. Two months' duration. (Randall Journal-Lancet.)

OTOLOGY

By Francis L. Lederer, M.D.

Deafness

Prevention—Appreciation of the social and economic importance of deafness has led investigators to dwell more and more on the prevention and alleviation of hearing impairment. Schools, through the co-operation of special organizations, health authorities and physicians, are conducting hearing surveys where defects may be discovered and remedial measures applied early enough to expect practical benefits to result. With few exceptions, hearing impairments detected early in the course of the disease, whether it be child or adult. proper and persistent treatment and the elimination of the underlying pathologic causes will either cure or improve the condition.

Mandatory tests in many States have won the approval of State and National medical societies. In a survey conducted in Albany, N. Y., E. M. Freund²⁰ finds that from 5 to 20 per cent have a hearing impairment. In addition to the tests of hearing, histories were studied, physical defects in the ears, noses, throats and sinuses were noted. Tonsils and adenoids were found not to be the only factors concerned in the production of deafness.

Complete obstruction of the eustachian tube causes acute middle ear symptoms and often abscess Partial obstruction in children causes a progressive loss of hearing, beginning with the high tones and gradually involving the low tones. If the causal condition is recognized and properly treated before the age of 15, hearing usually returns to somewhere near the normal level. After this age the results are far less satisfactory, because hyperplastic lymphoid tissue and partial tubal obstruction usually date from early

childhood. After the age of 15 the secondary changes in the middle ear may be so advanced that they can be repaired by no treatment whatever.

A long-continued partial obstruction of the eustachian tubes in children was found by S J Crowe and J. W. Baylor²¹ to cause retraction of the tympanic membranes, impaired hearing for high tones with relatively good hearing for low tones, and sometimes a total loss of hearing by bone conduction. This revolutionary statement is based on detailed observation of 60 children, in some cases for 10 years. In all of them the pharyngeal orifices of the eustachian tubes were partially occluded with nodules of lymphoid tissue This condition in the nasopharynx is identical with granular pharyngitis but is more difficult to see The location of the hyperplastic lymphoid tissue interferes with the normal function of the tubes The most satisfactory method of treatment is irradiation with radium or roentgen rays After the hyperplastic lymphoid tissue has been reduced and the tubal orifices look normal when viewed with the nasopharyngoscope, the hearing for high tones and for bone-conducted sounds often returns to the normal level. and it remains there so long as the eustachian tubes are clear. After a cold the original condition may recur, with consequent loss of hearing This proves that impairment or even total loss of hearing for high tones and for boneconducted sounds does not necessarily imply an inner ear or nerve lesion

Irradiation does not permanently remove hyperplastic lymphoid tissue, but relatively small doses, which in no way injure the pituitary gland, nasopharyn-

geal mucosa or inner ear, keep it in abeyance during the age period in which it grows most actively.

The authors concluded from their studies that the commonest type of middle ear deafness in adults begins during childhood. It often progresses so gradually and insidiously that it may not become evident, i. e., the frequency range of speech is not involved, until it is too late to correct the primary trouble and restore the hearing. They feel that if school children in the primary grades were examined with a nasopharyngoscope at least once a year and those with hyperplastic lymphoid tissue in and around the orifice of the eustachian tubes were treated with radiation as often as necessary to insure normal functioning of tubes, the number of deaf adults in the next generation could be reduced by 50 per cent

Studies of pupils of the Pennsylvania School for the Deaf were carried out by W. Hughson and his coworkers, A. Ciocco and C Palmer ²² Complete lack of response to auditory stimulation was found to be a rare condition, the children responding to at least 1 tonal frequency by air conduction in 1 ear and 85 per cent in both ears. In the great majority of these children the loss of hearing was bilateral and approximately equal in the 2 ears Sex was not a significant factor nor was age related to the degree of hearing loss Fifty-four per cent of the children were said to have been born deaf, the highest number at 1 year of age, decreasing rapidly at each successive age Meningitis was the most frequent contributing factor (about 17 per cent), with measles, otitis media, scarlet fever and head trauma accounting for one-half of the impairments. The authors offer no apparent association between auditory thresholds and the stated causes of deafness. A significant number of children was found to have enough residual hearing either by bone or air conduction to warrant some rational effort toward therapeutic relief.

Medical Treatment - Hormones and glandular products have been used in the treatment of deafness by various investigators and by several routes of administration. Mortimer and his colleagues²³ report the results of the insufflation of estrogen intranasally in a series of 55 cases of constitutional deafness Of the patients treated between July, 1936, and September, 1938, there are 39 females and 16 males. The cases were mostly diagnosed as either "otosclerosis" or "nerve deafness"; no attempt was made to select any given type of case. The patients range in age from the second to the sixth decade of life Treatment consisted of daily nasal insufflation of 1 cc. of oil containing 1000 international units of estrogen None of the patients was treated for less than 3 months Many of them have been under treatment for 6 months and there are some who have been treated intermittently for 2 years. As controls, 8 males and 6 females have been observed. Before and during the treatment, at intervals of from 1 to 2 months, the hearing acuity in each ear of each patient was measured Statistical examination shows that when all the data for 512, 1024, 2048 and 4096 cycles are considered, the hearing of the treated males improved slightly, while that of the untreated males deteriorated slightly. At these same frequencies the hearing of the treated females also improved slightly and of the untreated ones it appeared to deteriorate.

The *thyroxine* treatment of otosclerosis was first advocated by Gray in Great Britain and studied most extensively in this country by Goldstein ²⁴

The method has not been widely accepted to date, however. Thyroxine is used in the form of tablets, ½ grain (0.001 Gm.). One tablet is dissolved in 4 drops of warm sterile distilled water and injected directly into the middle ear cavity so that it may come in contact with the promontory and oval window. Any syringe and bayonet-bent needle may be used.

For anesthesia, an aniline-cocaine hydrochloride solution (chemically pure aniline 90 parts, cocaine hydrochloride 10 parts) has been recommended. Five drops are instilled into the ear for 5 minutes and then the remaining solution carefully wiped out

The site of injections is at a point halfway between the tip of the handle of the malleus and the posterior rim of the annulus tympanicus. Immediately after injection the patient sits erect and with the head thrown well backward keeps the mouth open for 3 minutes. This position keeps the fluid from escaping down the eustachian tube and also insures bathing the region of the round window. Following injection, the patient remains quiet for from 20 to 30 minutes and is not too active the rest of the day.

The treatment consists of 4 consecutive injections made alternately in the right and left ears at intervals of 1 week. This allows a period of 14 days in each ear for the absorption of the thyroxine solution.

G Selfridge²⁵ has used nicotinic acid, nicotinamide and quite recently sodium nicotinate in the treatment of some 30 cases of high-tone deafness. The ages of the patients ranged from 21 to 77 years. In many the results are striking; in all cases in which the audiogram shows a gradual decline of the tone scale, use of these fractions is justified, for, while the improvement in the audiometric curve may not be great, the

physical and mental improvement is sufficient justification. Indeed, any measure tending to ward off senescence is justifiable, and evidence is slowly accumulating that several components of the vitamin B complex play a definite part in the advancing of age.

Selfridge²⁶ also studied the eighth nerve in relation to thiamin chloride and nicotinic acid. He found the thiamin chloride was an essential addition to nicotinic acid for the increase in hearing. It was evident that the greatest improvement came from the use of nicotinic acid or sodium nicotinate, and only rarely was the improvement due to thiamin chloride, rather than nicotinic acid. Dysfunction of the endocrine glands. vitamin deficiency and any abnormal level of the electrolytes and any lowering of protein intake should be cor-Obviously the dietary intake should be kept up to the optimum level. especially during pregnancy, infancy, childhood and adolescence.

Davis and Rommel²⁷ report that the use of *prostigmin* in acute and chronic deafness and tinnitus aurium brings about definite and marked improvement. The value of prostigmin in these disorders was systematically investigated after the accidental discovery of Rommel that the ticking of a bedroom "tickless" clock (ordinarily no louder than a watch) was clearly audible to him at a distance of 8 feet following an injection of prostigmin which he had taken for other reasons

Twenty-eight patients with tinnitus aurium and acute blockage of the eustachian tube, most of whom had marked deafness, were given injections of 1 cc of prostigmin methylsulfate, 1:2000 solution, at intervals of 3 to 5 days, supplemented in most instances by catheterization of the eustachian tube and by massage. There was rapid remission of

the annoying symptoms, and few patients required more than 5 injections even when there had been loss of hearing for as long as a month But 2 patients had recurrence of their symptoms, and in each case 1 injection of prostigmin was followed by prompt improvement. In 2 acute cases prostigmin alone was used with satisfactory results. In the 1 case all head noises disappeared after 3 injections and in the other tinnitus disappeared after 4 injections.

Davis and Rommel discuss the reason for prostigmin's effectiveness in deafness They point out that the muscles of the ear and of the face have a common embryonic origin and a common innervation (trigeminal and facial nerves). Since the facial muscles in myasthenic patients regain normal function after the use of prostigmin, it is suggested that a somewhat similar phenomenon may occur with the otologic muscles in deafness after a dose of prostigmin This might also explain the beneficial action of prostigmin in trigeminal neuralgia. They caution against the use of large doses or too frequent administration, lest toxic effects be produced.

Vertigo

Vestibular Tests-Vertigo, being somewhat of a cerebral sensation, has usually been classed as a neurologic symptom According to B. H. Shuster, 28 with the more frequent employment of the labyrinthine or vestibular tests, the symptom vertigo has gradually become associated with otologic problems. Vertigo, as a subjective sensation disturbed equilibrium, frequently accompanied by slight obscuration of consciousness, may be manifested in the form of (1) giddiness, which is a mild degree of fainting; (2) sense of rotation and (3) pulsion, veering the person to one side or another. All of the foregoing

occur in attacks and are not continuous or constant. Shuster discusses the physiology of the labyrinth, the probable pathways for the production of vertigo and its etiology. The etiology is considered in 4 groups, viz.: (1) General systemic condition. (2) ocular conditions; (3) diseases of the ear, and (4) diseases of the brain These are discussed in considerable detail, and diagnosis as well as treatment is predicated upon a careful history and a thorough investigation and elimination of all of these factors.

The tests carried out for the examination of the vestibular labyrinth must be performed by those thoroughly trained in the technic and interpretation. J. L. Maybaum²⁹ finds vestibular tests are of considerable assistance in the diagnosis of brain stem lesions and particularly in the localization of expanding intracranial lesions. He points out that they are useful: (1) In the differential diagnosis of peripheral and central lesions of the eighth nerve; (2) in the differential diagnosis of an infra- from a supratentorial lesion, (3) for a more definite localization of a posterior fossa lesion (cerebellum, pons, cerebellar peduncles, pontine angle, etc); (4) in the early diagnosis of cerebello-pontine angle neoplasms, (5) as aids in localization by exclusion; and (6) for the evaluation of Meniere's syndrome.

Aviation and the Ear—W. Salem³⁰ says that at the otorhinolaryngologic clinic of the school of naval aviation in Rio de Janeiro they have about 200 records pertaining to examinations of the labyrinth of aviators. In the course of these examinations and of continuous control tests on aviators it was found that life as an aviator rapidly fatigues the organism and influences the vestibular apparatus. The more active the man is as a pilot, the weaker become his ves-

tibular reactions The rotatory test of Barany is employed by the author only during the first examination; for experienced aviators he found the test of little value. He observed that the postrotatory nystagmus should not be interpreted by algebraic formulas and he gained the impression that it is advisable to adhere to the general medical principle that an isolated sign never has absolute value. The falling test, with the head inclined 90 degrees forward, he found of no clinical value, but he regards the caloric test as the best mode of examination of the labyrinth. He cites cases of hypoexcitability in experienced pilots and says that to him such hypoexcitability is of no clinical value such pilots have no other symptoms, they can continue their activity as aviators.

The aviator acquires a sense of equilibrium superior to the normal. Aside from this, the labyrinthine sensitivity is nearly always diminished; this seems to be a phenomenon of adaptation By itself hypoexcitability does not reveal a perturbation of the labyrinth and has no value in aviation. The author also mentions a case of labyrinthine hyperexcitability detected by caloric tests in a stunt flier. This man was permitted to continue ordinary flying but was advised not to do stunt flying and high altitude flying.

On the basis of his observations the author reaches the following conclusions 1. There exists a labyrinthine adaptability in aviators which modifies the reactions in the examinations on the vestibular apparatus. It is a relative modification and of no pathologic significance in aviation 2. The labyrinthine hypoexcitability or hyperexcitability cannot be given uniform interpretations, but they must vary relatively in each case and in relation to each form of flying

Experiments have shown that prolonged stimulation of the ear by intense sound causes cochlear degeneration resulting in deafness. At first this deafness gradually wears off after a few hours, but constant flying without protection for the ears leads to permanent impairment of hearing.

E. D. Dickson, et al, 31 say noise in connection with flying arises from 3 sources, the engine exhaust, the propeller and the wind (slip stream) Tests were made to determine the amount of protection of hearing provided by the standard pattern of flying helmet and other ear protectors and also to determine what protection can be afforded by simple ways of blocking the ear or packing the meatus They learned that packing the meatus with absorbent cotton smeared with petrolatum was a quick, safe and efficient method. Audiograms of aviators using a helmet of the high altitude type with the ear phones attached showed no loss for high tones. The effect of noise on the ear seems to depend to some extent on the relative position of the aviators in the airplane If the aviators sit well forward and in front of the engines, the effect is considerably less severe than if they sit below or between the engines. Investigation is being continue in the hope of finding still more inve methods of protecting the ears of aviators

Meniere's Syndrome—C S Hall-pike and H. Cairns³² describe the microscopic changes in the temporal bones of 2 patients with Meniere's syndrome. In each of these the affected temporal bone showed a gross distention of the endolymphatic system together with degenerative changes in the sensory elements. A possible explanation of this distention is suggested by the absence in both patients of the normal area of perisaccular connective tissue around

the saccus endolymphaticus. A possible mechanism is further suggested whereby the microscopic changes may be correlated with the clinical features of the disease.

M. N. Fawcett and T. Cawthorne³³ studied the effect of various salt and fluid intakes on the symptoms of Meniere's disease in 11 cases. All but 1 were affected to a greater or lesser degree by variations in the intake of fluid and salt. Any steps taken to favor the retention of fluid within the body resulted in an aggravation of the symptoms, whereas the reverse was true when excretion of fluid was encouraged. In 9 cases this fluctuation of the symptoms was accompanied by variation in the hearing capacity, thus, when the symptoms were more marked the hearing was worse and vice versa of the patients under review tended to retain fluid unduly, although they were all sensitive to variations in the salt and fluid intake. It seems that imperfect functioning of the pressure-regulating mechanism of the endolymphatic system places the affected labvrinth under the influence of any factors that may effect the secretion or absorption of endolymph on that side. It is not unreasonable to suppose that an increase of the fluid content of the body may favor an increase of the intralabyrinthine pressure It is recommended that an antiretentional regimen should form part of the investigation of every patient with Meniere's disease.

While a great deal of work has been done on the pathology and treatment of Meniere's syndrome, H. Brunner³⁴ does believe the results to be proportionate to the effort applied. A Meniere's attack consists of (1) cochlear symptoms (tinnitus, deafness); (2) labyrinthine symptoms (dizziness, spontaneous nystagmus, diminution of the excitability

of 1 labyrinth), and (3) general vasomotor symptoms. In order to avoid confusion in the diagnosis, it is important to keep this triad of symptoms in mind. The symptoms may not all be present simultaneously in a single attack, but an exact diagnosis is only justifiable when the triad is present.

Between attacks, a retracted, fibrous, or atrophic drum may be found. An attack usually produces an acute increase of deafness which outlasts the attack. Dizziness and spontaneous nystagmus, between attacks, may or may not be present and an examination of the labyrinth usually reveals a hyperexcitability, 1 side more than the other. Failure of 1 labyrinth to react has rarely been observed

Treatment—Elimination of foci of infection, keeping open of the eustachian tubes, a salt-free diet, administration of bromides, iodides and calcium, faradization, reduction of fluid intake, and division of the vestibular branch of the eighth nerve all have their enthusiasts. Brunner states that he well realizes the many unsolved problems in connection with the entity but believes that scientific progress depends upon such conditions as Meniere's syndrome, for which much more investigation must be carried out.

Head Injuries and the Temporal Bone

Types—Fractures of the base of the skull more frequently involve the ear than fractures of the vault Fractures of the ear and mastoid are usually of 1 of 3 types. (1) Longitudinal; (2) transverse, (3) rupture of the petrous apex. The longitudinal type involves the tegmen tympani and runs forward through the roof of the eustachian tube. They may either be linear or branched and usually do not involve the labyrinth di-

rectly but may extend posteriorly into the mastoid and cause a rupture of the lateral sinus which will be manifest by free bleeding into the middle ear (hematotympanum) and into the nasopharynx. The transverse type begins in the region of the jugular bulb or base of the mastoid, crossing the petrous pyramid and ending on the anterior surface of the petrous bone In this type the middle ear and labyrinth are usually involved, producing mastoiditis or/and meningitis. According to W. E. Grove,³⁵ the middle ear is spared in one-half the cases but when injured, the damage affects only its medial wall (eustachian tube, knee of the facial canal and the footplate of the stapes)

Signs and Symptoms—The diagnosis is discussed by J. W. Fowlkes,³⁶ depending upon the part of the temporal bone involved The general symptoms are nausea, vomiting, headache, loss of consciousness, bloody discharge into or from the middle ear, sometimes accompanied by the escape of cerebrospinal fluid If a fracture is present, it may be evidenced by a lusterless drum which has taken on a bluish tint (hematotympanum). Pus may be found in the discharge from the canal and it is of importance to ascertain whether or not a chronic suppurative otitis media existed before the accident. In such a case, the complications of mastorditis, lateral sinus thrombosis or meningitis may develop and require surgical interference When the labyrinth is affected, the patient complains of vertigo, tinnitus, deafness, and nystagmus will be found present.

The roentgenological demonstration of the longitudinal fracture, according to Grove, offers many difficulties even when carried out early and after a month or 2 becomes practically impossible. The transverse fracture can usually be delineated in the film, often when even very slight, and this may hold true many years after injury. Grove reports 1 demonstrable 8½ years after the trauma.

A study of the after-effects of head injury is presented by W. F. Schaller,37 who believes that the term "traumatic neurosis" should be discarded and replaced by a more fitting and descriptive classification. After-effects of head injury may be classified as contusion, concussion, psychosis, and psychoneurosis, all essentially different conditions. The post-traumatic concussion state produces reversible changes of brain function which, in severe cases, may become irreversible, with demonstrable pathologic change. The post-traumatic psychoneurotic state, characterized by fear, suggestion and wishful thinking, is due to the precipitation of psychic complexes, following a period of meditation, in patient presenting inadequate personality traits and subjected to adverse mental influences.

In an analysis of 211 cases of skull fractures involving the ear, W. E. Grove³⁸ reports 49 miscellaneous fractures of the vault, face and sinuses, 146 longitudinal fractures of the temporal bone and 16 fractures of the petrous pyramid There were 7 cases of late hemorrhage from the ear after basal skull fractures and an escape of cerebrospinal fluid in 8, a sign which indicates that the subarachnoid space has been opened, usually associated with a longitudinal fracture. Facial paralysis occurred in 31 25 per cent of petrous bone fractures and in 18.7 per cent of longitudinal fractures. The paralysis was permanent in 207 per cent of cases Objective vestibular disturbances were encountered in 75 per cent of the cases. irrespective of the type of fracture.

Complaints and disturbances in the organs of hearing and balance observed in cases after head injuries were dis-

cussed by A. Alexander and R. Scholl.³⁹ The authors examined 231 cases of concussion of brain, 27 cases of contusion of the brain, 22 cases of fractures within the facial skeleton, 40 cases of fracture of the vault of the skull, and 67 cases of fracture of the base of the skull. About 30 per cent of these cases had complaint referable to the cochlea and The complaints about the labyrinth. tunnitus and diminution of hearing are dependent upon the severity of the injury, as they are more frequent in cases of severe involvement than in slight injuries.

In contrast, the complaints about dizziness are more or less independent of the severity of the injury, inasmuch as they are to be found in severe as well as in slight injuries. Dizziness is more frequently complained of than difficulty in hearing, the relationship being about 40 to 60 per cent. The objective exammation in about 33 per cent of the cases reveals a disease in the middle ear or in the cochlea, and in 30 per cent of the cases a disease in the labyrinth Similar to the subjective symptoms, the percentage of objective diseases of the cochlea increases with the severity of the Therefore, only 15 per cent of cases of concussion of brain on exammation evidence a disease of the middle ear or the cochlea

In contrast, this percentage is 80 per cent as far as the fractures of the base of the skull are concerned. In other words, every seventh case of concussion of the brain with the complaint of timitus or diminution of hearing has a disease in the middle ear or in the cochlea which can be demonstrated clinically. In contradistinction to the cases of fracture of the base of the skull, who complain of tinnitus or diminution of hearing, four-fifths have a disease in the middle ear or the cochlea. Looking upon all cases

of injuries of the skull, there are 5.2 per cent of cases evidencing disturbances within the cochlear apparatus, even in clinical examination. These difficulties are most often produced by a disease of the internal ear (about 60 per cent) which appears either immediately after the injury or late afterward. Complete deafness after an injury is relatively rare. It was found present in 0.26 per cent of the cases who had difficulty in hearing

In a review of 19 unselected cases, M. Rosenthal⁴⁰ suggests that impairment of hearing does not follow injuries to the head as commonly as is generally accepted, but that the trauma most often occurs in the basal coil of the cochlea with impairment for perception of the higher frequencies, above 2048 double vibrations, which does not, by itself, produce "functional" loss of hearing.

Treatment—Excellent contributions on this subject have been presented by N P. Battle,⁴¹ P Shapiro and H. Jackson,⁴² Browder and R Meyers,⁴³ M A Zacks,⁴⁴ H B. Perlman,⁴⁵ A W. Adson,⁴⁶ W E Grove,⁴⁷ and A P Hofman,⁴⁸

Patients should be *put to bed* and kept there longer than it appears necessary, the minimum, 4 to 6 weeks. In the beginning, *shock* should be *treated*, *lacerations sutured*, reduction of other fractures may wait because added manipulations must be avoided X-ray diagnosis is not to be indulged in when shock is present. The blood pressure and respiration must be closely watched, as indications may arise from a change in treatment or operation

Treatment of shock, which is so necessary in head injuries, is of utmost importance. While there is controversy about the administration of fluids, blood chemistry studies have proven that marked

alkalosis may be present before signs of dehydration appear, and in such cases fluids must be given as indicated, with caution to guard against edema of the brain. Spinal puncture is employed to relieve edema of the brain due to stasis of the blood because the circulation is blocked, with increased pressure of the spinal fluid, hemorrhage, and ischemia.

If blood or spinal fluid is found coming from the external auditory canal, it should not be interfered with under any circumstance, as there is nothing to gain and bacteria may be introduced, thus producing a meningitis The skin around the area should be kept clean and a large sterile mastoid dressing applied hematotympanum is present, the tympanic membrane should not be incised. If the discharge becomes secondarily infected and mastorditis develops, any form of operation should be postponed until absolute indications present themselves (fever, chills, headache, mastoditis, etc)

Otitis Media

Etiology — In another communication regarding swimming and otitis media, H. M. Taylor⁴⁹ has for many years contended that biology is the fundamental study of the phenomena of life in all its varied relations. After recognizing the facts pertaining to the adaptations that aquatic animals have for protecting the drum membrane against water and realizing man's lack of like modifications, one can hardly escape the conclusion that a perforation of the drum membrane is in man a positive contraindication for swimming or diving.

Otitis externa, or furunculosis, from which the swimmer often suffers, likewise illustrates that the external auditory canal was not intended to withstand the vitiating effect of water. If the hand is immersed in sterile water for 30 minutes,

the skin will be wrinkled and degeneration of the epithelium will result. A similar change takes place in the ear of the swimmer. Maceration of the delicate dermis by the water breaks the skin and opens to the ever-present staphylococcus an avenue of infection, with resulting various forms of otomycosis, frequently observed during the swimming season.

Infections of the ear or sinuses secondary to swimming evidently come from one or both of these sources: Foreign bacteria may gain entrance to the deeper portions of the nasal apparatus and the conjoined structures; or bacteria normally and constantly in this region may be allowed, by a lowered resistance on the part of the swimmer, to multiply to pathologic proportions

In view of the modifications that aquatic animals have for their environment, i e, for preventing water from gaining entrance into the upper part of the respiratory tract and into the external auditory canal and for maintaining a normal body temperature in cold water, provisions that man conspicuously lacks, there is but 1 conclusion, that man is essentially a terrestrial animal and that his anatomy and physiology are not modified for an aquatic environment When out of his normal sphere, unless he takes cognizance of the limitations nature has placed on him and heeds the fundamental laws that regulate his being, he subjects himself to the likelihood of contracting the infections that frequently beset the swimmer. These nasal and aural involvements run the gamut of pathologic conditions from the innocent circumscribed furuncle to a diseased condition of the mastoid, with all its intracranial complications, as well as the fulminating infections of the sinuses and such complications as osteomyelitis of the frontal bone and intracranial lesions

Pathogenesis—In discussing the diagnosis and treatment of diseases of the ear in children, H. J. Williams⁵⁰ states that certain anatomical facts must be known by the practitioner to enable him to understand why middle ear inflammations in the infant and child differ from those occurring in adult life. The highest percentage of both catarrhal and suppurative otitis media occurs in children before the fifth year and it is obvious that, if progress is to be made in the prevention of deafness, emphasis must be placed on the diagnosis and treatment of otitis media in this age group.

For the sake of clarity, let the age of infancy be up to 1 year. At that age, the anatomy of the ear differs from that of the older child. The auditory tube is short, being from 16 to 18 mm. long, but the breadth is equal to that of the adult. The pharyngeal orifice is on a level with the floor of the nose, and infected material consequently from the nose finds easy access to the tube. There is no angle or 1sthmus, and the tube is practically horizontal. The muscles are not well developed. In the infant the tympanic membrane is thicker and more elastic than in the older child. membrane often bulges when the infant

The osseous external auditory canal consists only of a bony ring which gradually grows outward by the deposit of bone on its outer surface. The drum is at an acute angle with the canal and the walls of the membranocartilaginous portions are studded with fine hairs, which make examination of the tympanic membrane difficult.

During the second year, the osseous canal begins to assume the adult form. The lumen of the canal becomes larger, and the tympanic membrane becomes more horizontal.

The middle ear usually becomes involved in acute infections of the upper respiratory tract and the exanthemata. particularly scarlet fever and measles. There is a rise in temperature and the pain is usually severe. The tympanic membrane is at first red and then bulges in the posterior half. Early free linear incision is advocated by Williams because in a study of 14,733 scarlet fever cases, 1535 of whom had otitis media (the total number of ears was 2186), 858 had an incision of the drum. In this group, 6.6 per cent developed surgical mastoiditis, whereas 9.3 per cent required surgical interference in the group which had spontaneous ruptures. In a series of measles complications, 11 per cent developed surgical mastoiditis following spontaneous ruptures. Adenoids and tonsils and sinus infections are shown to be definite predisposing factors in the production of otitis media.

Treatment-This past year has produced no new trends in therapy, but some interesting controversial discussions concern incision of the tympanic membrane and the use of what the year before was hailed as the miracle drug. In the interpretation of all of these, it is necessary to bear in mind that the antagonists of incision may not be considering the entities which actually require release of intratympanic pressure from a humane point of view, to say nothing of the therapeutic advantage of selecting a site for drainage in the tympanic membrane which insures a better prognosis for life as well as for the prevention of complications. The employment of sulfanilamide or its derivatives was bound to meet with disappointments due to failures and complications from its use because it was empirically prescribed without an evaluation of the clinical signs or regard for the untoward effects of the drug.

Clinical observation over a period of has led H. Bakwin vears H. Tacobziner⁵¹ to believe that incising an inflamed drum often leads to a purulent discharge in an ear in which, if there were no operative intervention, the infection would subside spontaneously. Furthermore, the results over a period of 5 years strongly indicate that frequent examinations of the ear, by traumatizing the drum and the canal and by exposing the nasopharynx of the infant to the expired air of the examiner, favor the development of purulent otitis media. In many pediatric hospitals, otitis media is treated casually and its management is left to the house officers without adequate supervision by the visiting staff. This attitude is fraught with danger, as it exposes children already ill to the danger and inconvenience of unnecessary paracenteses and purulent otitic discharges. Though disease of the mastoid is uncommon in infants, it does occur and is to be avoided if possible. By careful supervision, strict adherence to a standardized set of indications for myringotomy and the avoidance of too frequent examinations, the incidence of purulent otitis media may be reduced and the danger of disease of the mastoid The authors state that the results of their study lend no support to the view that delay in incising an ear drum is harmful to the child. When doubt exists, they believe that it is preferable to wait In acute intestinal intoxication, when a specific relationship to acute purulent otitis media has been hypothesized, the incidence of aural discharge has been reduced to one-third during the 5 years under discussion, with a fall rather than a rise in case fatality from this serious disease

In the treatment of the suppuration following incision or spontaneous rupture, discussion always centers about the advantages and disadvantages of the "wet" and "dry" treatment in cleansing an acutely suppurating ear, some otologists even suspecting that irrigation of an ear spreads infection to the mastoid cells. Usually, inflammatory conditions of the middle ear and the mastoid cells exist simultaneously, and O. C. Hirst⁵² does not believe that it is possible under ordinary circumstances to carry infection to the mastoid cells by douching the middle ear. He recommends the mercurials of the orthocresol group, alone or with alcohol, as satisfactory irrigating solutions. Hirst used the anhydride of 4, nitro-5 hydroxymercuriorthocresol(metaphen), containing about 56 per cent mercury, in a dilution of 1:10,000 every 2 or 3 hours After the acute condition has subsided, usually in 7 to 14 days, alcohol is added, beginning with 35 to 40 per cent and increasing the strength up to 95 per cent. While Hirst recommends a simple mastoidectomy as a preservation of hearing after an ear continues to drain for more than 8 weeks, most authorities would feel that indications for operation must be predicated on the presence of other signs and symptoms.

Silver picrate solution (½ to 1 per cent) instilled into the canal is advocated by V. R. Vanstane.⁵³ The canal is first thoroughly dried and then filled with the solution.

In accordance with the growing tendency to broaden the scope of radiation as a therapeutic procedure, the utilization of radiation therapy in otitis media has led certain clinicians to laud the efficacy of this modality J. P. Brown and his coworkers⁵⁴ state that the roentgen treatment of acute and chronic otitis media is rational because of all the body cells the lymphocytes are the most sensitive to the rays Lymphocytic infiltration is a major and constant feature of inflammation and infection of the middle

ear, and breaking down these cells relieves pressure within the cavity and thereby relieves pain.

Roentgen irradiation also promotes phagocytosis, which progresses rapidly until the lymphocytes are almost entirely destroyed. The polymorphonuclears and eosinophils undergo disintegration somewhat less rapidly. In addition to this cellular destruction and phagocytosis, the x-rays are believed to liberate enzymes, antibodies, and other unknown principles which also aid in the processes of autolysis and liquefaction.

The technic that the authors employed has varied. At present they are using 85 kilovolts (peak), 5 milliamperes, 16inch target-skin distance, and 1 mm. of aluminum filter They do not follow a hard and fast rule as far as dosage is concerned but take into consideration the severity or duration of the condition and the age of the patient In mild cases in infants they have used from 50 to 60 roentgens and in young children and adults the dosage has varied from 60 to 100 roentgens Their cases of acute catarrhal otitis media required only 1 treatment. In cases of acute purulent otitis from 3 to 7 days elapsed between treatments, depending on the condition of the ear Patients with chronic purulent offits received treatments about 10 days apart.

In acute otitis media, if the temperature was not more than 99.6° F. (37.5° C), with bulging of the drum and obliteration of the short process, irradiation was not preceded by myringotomy. Only 1 of 31 cases of acute catarrhal otitis media required myringotomy following therapy and in this instance myringotomy had been refused by the parents and roentgen therapy was tried as the only resort. The majority of the cases was seen within the first 24 or 48 hours. The average number of roentgens was

72.9 and the number of days required for the drum to return to normal was 3.15. Of 18 cases of acute purulent otitis media, myringotomy was performed in 12, while spontaneous rupture of the drum membrane occurred in the other 6 within 24 hours of being seen. The duration of symptoms before the first examination varied from 3 days to 6 hours These patients received an average of 1 33 treatments, with an average of 70 roentgens. The ears were dry and the drums were normal within an average of 8.16 days.

In conclusion, the authors state that instead of mastoidectomy, it now seems that not only will a short series of roent-gen treatments suffice to cause an ear to become dry and free from pain, but hearing will be fairly normal in it. None of their cases has shown any complication following this mode of therapy.

In a review of the literature and from his own observations, B. R. Dysart⁵⁵ believes that x-ray treatment of acute inflammatory conditions of the ear and mastoid shows much favorable and little unfavorable evidence. He believes treatment should be started early and that small doses produce better results than large doses which may even be harmful

Sulfanilamide Therapy — Because of its tendency to obscure the clinical course of the infection, J. L. Maybaum and his associates 56 believe that sulfamlamide should be used cautiously if at all in acute otitis media. It is contraindicated during the course of suspected mastoiditis before operation and also after operation unless meningitis, sinus thrombosis or cerebral abscess complicates the disease For the present, at least, they believe that the indications for its use are as follows Sulfanilamide may be given in otitis media before suppuration sets in. However, otitis media of this type commonly proceeds to spon-

taneous resolution. Occasionally, in cases of extreme bacterial meningitis (streptococcic or pneumococcic), intensive administration is indicated before operation (24 to 36 hours) and then postoperatively. Sulfanilamide should be given in sympathetic meningitis secondary to an extradural abscess, an abscess of the brain or labyrinthitis. In thrombosis of the lateral sinus sulfanilamide should be followed by thorough surgical intervention and continued postoperatively.

The drug is especially useful in instances of continued otitic sepsis, even though a thorough operative procedure has been previously performed. In petrositis, sulfanilamide should not be administered during the period of observation because of the danger of masking the clinical course and thus interfering with the proper management of the condition. If operation is indicated, sulfanilamide should be given promptly in the usual manner. Indiscriminate use of sulfanilamide may result in latent forms of infection of the middle ear or the mastoid and their complications That the sulfanılamıde tends to mask the clinical picture of otitic infection has been observed often A striking example of latency due to the administration of sulfanilamide was recently reported by Smith and Coon, who stated that a moderate dose of sulfanilamide may partially control meningitis so that it presents an unfamiliar clinical picture

Inadequate sulfanilamide therapy has been followed by recurrence of otitic infections with beta-hemolytic streptococci, according to J. M. Converse. The believes that the laboratory studies which are required for the effective use of sulfanilamide necessitate hospitalization of patients under treatment. This form of therapy should be reserved for cases of spreading or life-endangering streptococcic infections. The enthusiasm for

specific chemotherapy is readily understood but is open to considerable criticism. The patient with meningitis is under hospital observation and treatment is continued until the spinal fluid has returned to normal. The patient with acute otitis media or mastoiditis receives sulfanilamide therapy only as long as there is persistent pain or discharge, and treatment is usually stopped on clinical instead of laboratory evidence.

Symptoms of mild toxicity, such as malaise, lassitude, weakness, headache, dizziness, depression, anorexia, and nausea, are frequently encountered in patients receiving sulfanilamide. Less commonly, tinnitus, mental confusion, paresthesias, dyspnea, inability to concentrate, diarrhea, constipation, and vomiting are observed Lowering of the carbon dioxide combining power is not uncommon. With rare exceptions, the drug can be given despite these manifestations and not cause concern. According to C. F Garvin.⁵⁸ moderately severe symptoms of toxicity, such as deep cyanosis, marked dyspnea, distinctly lowered carbon dioxide combining power, severe vomiting, diarrhea, abdominal pain, itching of the skin, and slowly developing anemia, indicate vigilance and possibly a reduction of dosage

Symptoms of severe toxicity, such as fever, dermatitis, acute hemolytic anemia, leukopenia, psychosis, or jaundice, demand immediate discontinuance of the drug Garvin suggests that the patient be closely observed, the blood be examined daily, the use of sulfates and other drugs be avoided and that sulfanilamide in patients with anemia, leukopenia, or hepatic damage is contraindicated. The treatment of these toxic manifestations consists of the immediate withdrawal of the drug, bed rest, forcing of fluids, blood transfusion, and other measures as are indicated, such as yellow

bone marrow extract, pentnucleotide, intramuscular liver, iron, oxygen, methylene blue, sodium lactate, Ringer's solution, dextrose, and insulin.

Acute Mastoiditis

Development—Observations on specimens from 27 infants and 69 human fetuses with reference to the origin and distribution of air cells in the temporal bone were made by T. H. Bast and H. B. Forester.⁵⁹ In an 8-week fetus, the eustachian tube extends to the middle ear. The connective tissue of the middle ear then becomes loose, and the epithelium from the tube invades it. This pneumatization of the middle ear is slow and not completed until late in fetal life The region of the antrum is first indicated in the twenty-second week of fetal life, when loosening connective tissue from the middle ear extends laterally between the tympanic plate and the otitic capsule in the region of the canal The periosteal bone of the capsule then grows around this connective tissue and unites with the tympanic plate in the twentyninth week of fetal life Soon after this. the epithelium from the middle ear invades the loose connective tissue of the antrum, which is well pneumatized by the thirty-fifth week

With the expansion of the antral bone and the tympanic plate to give rise to the region of the mastoid, the epithelium from the antrum invades the newly forming bone to form the mastoid cells. Some of these early cells later become incorporated in the enlarging antrum. Air cells from the antrum also invade the bone lateral to the semicircular canals to form the antral cells.

As the petrous bone develops, other air cells are formed in it. One large group can be divided into smaller groups, the subtubal, the postcarotid, the precarotid, and the precochlear. Another

group, the supracochlear, lies anterior to and above the region of the geniculate ganglion.

Mastoid cells as a rule open into the antrum, but occasionally they open into the middle ear directly. Antral cells open into the antrum; the carotid group open into the middle ear but the subtubal and precarotid cells may also open into the eustachian tube. The supracochlear cells may open into the middle ear or be continuous with the precochlear group. Intercommunication between cell groups may exist. Air cells do not extend into true bone marrow.

Climatic Factor—During 1938, 92 mastoidectomies were performed on children by the attending otologic staff of a pediatric hospital. N. D. Fabricant⁶⁰ selected 5 cases from this group to illustrate the influence on the clinical course of the ailment of daily meteorologic and seasonal changes. Simplified meteorographs have been prepared from the United States government meteorologic data; for purposes of simplification the high and low range of daily temperature were regarded as an adequate index of meteorologic change. From the data obtained, Fabricant concludes that mastoiditis is most often precipitated in the wake of a fall in atmospheric temperature (cold front or polar front), when the functional status of the mucous membranes of the nose and throat has changed He believes that the climatic factor in mastorditis, as expressed in terms of the weather and the season, can be measured with considerable accuracy

According to F. F. Agnew, 61 every case of otitis media is a potential mastoiditis and if purulent drainage persists for a period of 2 weeks or more, surgical measures should be considered, that more than 65 per cent of mastoids which are operated upon are due to a latent infection, aroused to activity when, by

some acute process, a fresh media is substituted for the old; that mastoiditis is as distinctly a surgical problem as is the acute appendix and deserving of like consideration; that the complications of mastoiditis are the result of unpardonable delay or wilful neglect; that if conservation of health and hearing are to be supplied to the public, the obstetrician, the pediatrician, and the general practitioner should give more intelligent consideration to the ears of the infant and the growing child.

Sulfanilamide Therapy-According to W. A Noble, 62 the use of sulfanilamide was successful in all but 1 of 24 cases of acute mastoiditis. The infection in all but one was due to Streptococcus viridans. There was a history of previous attacks of otitis media in 10 of the A history of measles preceding the otitis media was given by 5 patients, with scarlet fever as a predisposing cause by 1 A bilateral mastoidectomy was necessary in only 1 case Three of the 24 patients had acute recurrent trouble from 3 to 6 months after the simple mastoidectomy, which necessitated myringotomy and incision of the mastoid wound. The average number of days in the hospital following the simple mastoidectomy for the entire group was $11\frac{1}{10}$ days There was complete recovery of all but 1 patient, who died of acute purulent meningitis (Streptococcus viridans) and diabetes mellitus

According to V G Horan and S G French, 63 during the year following the routine use of sulfamilamide in otitis media, the ratio of acute mastoiditis to acute otitis media has been greatly reduced, from 227 to 45 per cent. The percentages were obtained from the statistical returns of the Royal Naval Hospital and the average for the years 1934, 1935, 1936, and the early half of 1937, when sulfanilamide was not being used.

is compared with the year comprising the latter half of 1937 and the early half of 1938, when sulfanilamide was used in a routine way. From January, 1934, to June, 1937, the number of yearly deaths from the complications of acute suppurative otitis media averaged 2.85, while from June, 1937, to June, 1938, there were no deaths from this cause. The authors make no claims with regard to the efficacy of the drug in the treatment of otitis media, but the figures are consistent with the view that it is a preventive of the complications of this disease. It is not claimed that every case of otitis media was streptococcic in origin, for swabs were not taken in all of them. All those in which swabs were taken proved to be due to a hemolytic streptococcus, and during the past winter and spring there has been, in the district from which these cases came, almost a streptococcus epidemic consisting of tonsillitis, scarlet fever (which has been severe), and the like. The sulfamilamide was used in a purely "shotgun" manner on admission The results seem to justify its use, for, even if the otitis does not respond to the treatment and mastoiditis develops, no harm has been done and the patient's resistance is in no way impaired by the drug In no case was the administration of sulfamilamide prolonged for more than 14 days Chronic otitis media has not been considered in this group of patients, as the majority of them had no previous record of otitis media.

Brain Abscess

Sixty cases of brain abscesses of all types, including those of metastatic origin, have been observed by J. F. J. King⁶⁴ since 1920 and a number of traumatic abscesses and brain fistulae was observed during the 4½ years' service with the German and American armies during the World War. Many

had been operated upon previously or tampered with before coming under the observation of the author Of these 60 patients, 29 died and 31 survived. Of the former, 8 were frontal, 8 were temporal, 3 were cerebellar and 10 metastatic (8 multiple, 2 single, all cerebral).

In 3 of the early cases in 1920 and 1921, tube drains were used before the open method was introduced; in 1 frontal, the tube became displaced and in an attempt by an assistant to replace it, the tube was placed into the brain substance outside the drainage tract; in 1 frontal, the tube perforated the ventricle; in 1 temporal, the tube was removed too early and a secondary pocket ruptured into the ventricle Eight were multiple, metastatic, and therefore hopeless; 2 were large, single metastatic abscesses, in which the dilated ventricle ruptured into the evacuated abscess cavity through the thin interval before the introduction of lumbar puncture to reduce intraventricular pressure Two were acute abscesses, 1 with blood stream infection of Staphylococcus aureus, and 1 patient was moribund and was tapped only to satisfy the family Six cases were complicated by suppurative leptomeningitis at time of operation, 1 bilateral frontal

Three were cerebellar, 1 patient died following mastordectomy, aspirated after death; 1 when seen was moribund due to jamming of the conus in the foramen after repeated lumbar punctures and extension by rupture of abscess against the pons; 1 was an early case in which the wire cone drain was used

One patient with frontal lobe abscess recovered from the original abscess and died later from a second abscess formed from reinfection, or lighting up of the infection in an improperly operated frontal sinus. Ventriculograms would have located this abscess

Four patients were operated upon according to the method advised and should have recovered but died as a result of mishaps or accidents: 1 temporal, in a 6-year-old girl who died of pneumonia following dakinization and being placed by an open window in the winter; 1 temporal, in which the patient, who was in a distant hospital, removed the dressing and tore the brain substance with her finger; 1 temporal, well walled-off, in a comatosed woman who had a temperature of 104° F. (40° C) and insufflation pneumonia, due to pouring eggnog down her trachea (at autopsy, egg and milk were found in the lungs); 1 temporal, in an unmanageable coast guardsman, who got out of bed on the sixth postoperative day, and the abscess ruptured into the ventricle One patient with frontal lobe abscess died before being seen following rupture into the ventricle

Of the 31 patients who survived, 8 had frontal abscess, 10 temporal, 5 cerebellar, 5 traumatic, and 3 metastatic, 1 of which was acute, operated upon on the sixth day after onset, and 2 were walled-off large abscesses. Four were not operated upon by the author; but operation, management, or both were under his direction. In 2, 1 frontal and 1 temporal, there was gross rupture into the ventricle, with associated meningitis, loss of consciousness, and loss of sphincter control.

Thirty-five patients were operated upon according to the methods described, 4 of whom died, 2 of preventable pneumonia, 1 from tearing the brain after removal of a dressing in a distant hospital, and 1 from rupture into the ventricle due to getting out of bed on the sixth day.

In all cases, only 1 operation for brain abscess was required Multiple procedures were never done No patient has

had postoperative convulsions except 4 who had convulsions before operation.

As experience with these cases has increased and earlier observation of the suspected brain abscess has been made, the better the results have been. The last 20 consecutive patients, with 1 exception, recovered.

Y. Meurman⁶⁵ believes that where a brain abscess is suspected, ventriculography is of great value and that the procedure ought to become more widely employed. It may help especially to locate the abscess in cases where the dura does not evidence the point of entrance of the infection. In cases with a large abscess, the introduction of a substance that produces a contrast into the abscess and the subsequent taking of an x-ray film will be of assistance in finding suitable areas for drainage. The changes in the ventriculogram in abscesses consist of dislocation, incomplete filling with air, in some cases a total lack of air in a part of the side of the ventricle or in the entire ventricle and at times a deformity of the ventricle. Meurman emphasizes the fact that abscesses of the temporal lobe and even those in the occipital lobe are able to markedly dislocate the anterior horns over to the healthy side

The relation of the histologic to the clinical features in abscess of the brain was discussed by B J Alpers 66 He studied the histology and bacteriology of 27 abscesses of the brain Their histologic structure is described, especially with reference to the formation of the capsule of the abscess Time, the type of organism and the resistance of the host are the most important factors in the development of the capsule. The optimum time for the formation of the capsule formation is 3 to 4 weeks. The abscess is composed of (1) a necrotic zone (cavity), (2) a reactive zone, (3) a fibrous zone, and (4) an encephalitic zone. The fibrous or connective tissue capsule takes its origin from the following sources: (1) The blood vessels, (2) the lymphocytes, and (3) the dura and pia mater (in cases of trauma).

Headache, secondary to disease of the ear, is discussed by K. M. Simonton, 67 who reports epidural abscess in 2 cases following radical mastoid operation. The pain of acute mastoiditis is usually limited definitely to the region of the ear and mastoid process. It tends to be continuous and relieved by measures which promote free drainage from the infected mastoid cells. Headache associated with disease of the mastoid cells, in contrast to pain, frequently centers around the affected ear but extends to other regions usually on the same side of the head It is often intermittent and tends to increase so much in the morning that the patient is awakened from a sound sleep Exacerbation of the headache in the morning is the result of the increase in blood supply to the intracranial structures It can be caused by (1) localized hyperemia or inflammation of the dura, (2) epidural abscess, (3) parisinus abscess, (4) sinus thrombosis, (5) subdural abscess, (6) pachymeningitis, (7) leptomeningitis, (8) encephalitis, (9) otitic hydrocephalitis, (10) abscess of cerebrum or the cerebellum, and (11) chronic petrositis Clinical observation, neurologic examination, roentgenologic, and laboratory studies usually will establish the diagnosis of the lesion and its approximate location.

Treatment — When the presence of intracranial complications is suspected, surgical treatment should be directed toward elimination of the disease causing the symptom. Even if the bone overlying the dura is not obviously diseased, according to Simonton, it should be removed purposefully when

headache is a prominent symptom, for the dura must be visualized in order that the surgeon can be certain that a lesion has not escaped his notice. Brain abscess, hydrocephalus, encephalitis, and meningitis should receive treatment appropriate to the condition.

Three cases of otogenous abscess of the brain with recovery following conservative management are reported by L. J. Adelstein. Two of the patients had abscess of the temporal lobe and 1 of the cerebellum. In all 3 cases the abscess was secondary to otitis media and mastoiditis. All the patients have been able to return to their former activities and have remained symptom-free. The necessity for careful neurologic study is emphasized, since the localization plays the most important rôle in successful supervision.

The principles and the process of encapsulation are discussed with reference to the axiom that abscess of the brain is not an acute surgical emergency. The optimum time for surgical intervention appears to be from 4 to 6 weeks after the initial cerebral involvement. The prevailing methods of drainage are discussed by Adelstein, who finds that the highest percentage of recoveries has followed dramage by simple methods by which excessive trauma and spread of infection are avoided. With a correctly centered trephine opening, a small dural incision, accurate and immediate location of the abscess and adequate and prolonged drainage, the formidable picture of cerebral herniation, cerebrospinal fluid fistula, with possible infection and brain fungus, is eliminated

In a study of a case of brain hermation, C Hall⁶⁹ surveys the literature and concludes that the complication is avoidable and the prognosis is dependent upon the coexisting pathology and the methods of treatment. The early

treatment of a brain hernia should be directed toward (1) the avoidance of trauma; (2) the prevention of infection. and (3) the lowering of intracranial pressure. Very light, nonirritating dressings should be employed Hall finds the intravenous administration of hypertonic solutions, such as 50 per cent glucose, is a rational procedure for lowering a pressure which is mainly caused by brain edema and is safer than spinal puncture Caustic solutions, alcohol, x-rays, and galvanocautery have not been effective. Compression only acts to increase the causative mechanism Removal is condemned because of the possibility of producing a meningitis, spreading encephalitis, hemorrhage or of opening the lateral ventricle. Herniation may recur after such a procedure and even be larger than before. The hernia becomes covered with skin without any grafting being necessary.

Sulfanilamide in the treatment of brain abscess and the prevention of meningitis was reported by P. C Bucy 70 Owing to an error in diagnosis a right cerebellar abscess was exposed with a bilateral suboccipital cramectomy The contents of abscess were aspirated and the surface of the cerebellum was contaminated with pus swarming with hemolytic streptococci, thus exposing the ventricular system and the subarachnoid space to this infection. The abscess was not drained The administration of sulfanilamide was begun at once. The patient improved steadily. There was almost no febrile reaction and at no time did signs develop either of meningitis or of refilling of the abscess. The patient had almost completely recovered within 2 In the future it is proposed to treat all brain abscesses in a similar manner; that is, make a defect in the skull over the abscess, aspirate the pus and

begin the administration of sulfanilamide. If this suffices, nothing further will be done. If not, the abscess will be opened, evacuated and drained as usual

Lateral Sinus Phlebitis

Statistics—A survey of current opinion and records was collected by W. H. Evans.⁷¹ A questionnaire addressed to approximately 1000 physicians and hospitals brought 343 replies. From this correspondence a collective series of 59,850 cases of mastoid disease was compiled with 1556 cases of thrombosis of the lateral sinus. These figures yield an incidence of 26 per cent for thrombosis of the lateral sinus in mastoid disease

Only 92 replies contained specific information regarding mortality. From these, a series of 979 cases of thrombosis was compiled, with 305 deaths, a mortality of 31.2 per cent.

In general, the incidence of thrombosis seems to be higher in children's hospitals and charity hospitals and in private practice largely among referred patients. There is no evidence from the statistics here assembled that climate has any influence on the incidence of thrombosis of the lateral sinus in mastoiditis, although it may affect the incidence of mastoid infection itself.

Otitic Hydrocephalus—In a presentation of 10 cases of increased intracranial pressure persisting for from 1 to 11 months after an acute otitis media, 7 cases being in young children, W. J. Gardner⁷³ attempts an explanation for the syndrome which is not due to meningitis, brain abscess or encephalitis. He believes the syndrome of increased intracranial pressure without localizing signs is usually due to sinus thrombosis, and that when the picture is associated with localizing cerebral signs and recovery ensues without suppuration, it means that the thrombus (perhaps sterile)

within the cranial sinuses has extended into the cerebral veins.

Gardner is not convinced, however, that the thrombus must necessarily extend into the sagittal sinus in order to produce increased intracranial pressure. Since the total volume of the intracranial fluid is usually not increased and there is no hydrocephalus, he attributes the increased pressure to engorgement of the intracranial veins, plus, in some cases, sterile subdural effusion resulting from a pachymeningitis.

Recovery from this state of increased intracranial pressure results when, by means of recanalization or the development of collateral circulation, the return of venous blood from the cranial cavity is once again adequate. Gardner values subtemporal decompression as a guide as to when a therapeutic lumbar puncture should be done and that it permits the evacuation of a subdural effusion, if one is present

Manometric Reading — An attempt is made by H R. Merworth and A. A. Clinco⁷⁴ to criticize unfavorably the routine use of jugular pressure in the determination of manometric readings during lumbar puncture.

They cite 9 cases (1 an ear case) to prove the futility of such a routine procedure and the potential danger of increasing the bad effects known to be associated with the injudicious withdrawal of cerebrospinal fluid

The Tobey-Ayer otologic application of the Queckenstedt phenomenon may demonstrate obturating sinus thrombosis. The test is negative (the manometer rises on jugular compression), when the phlebitis is not entirely obliterating. Its sources of error lie (1) In the difficulties of a proper technic in patients with thick necks, (2) in the disregard of the normal differences in spinal fluid pressure after separate compression of

the internal jugular veins; (3) in the low spinal fluid pressure of some patients; (4) in straining by adults or crying of children, and (5) in anatomic anomalies of the lateral sinus and torcular Herophili Cody⁷⁵ feels that these coefficients of error can usually be allowed for, and within limitations imposed by them, the spinal manometric test still retains a high value in sinus thrombosis.

Otitis media and mastoiditis simulating thrombophlebitis of the lateral sinus is discussed by M. S. Ersner ⁷⁶ When sepsis occurs in conjunction with suppuration of the temporal bone, one is led to believe that phlebitis and thrombosis of the lateral sinus are responsible for the sepsis in 100 per cent of the cases However, actually, the incidence of sinus thrombosis and phlebitis in otologic diseases is only 2 per cent. Each case of sepsis is entitled to deliberate and deep consideration from a medical and surgical standpoint

The elements concerned in the causation and manifestation are so numerous that it becomes easy to err. Therefore, the surgical treatment of the lateral sinus should not be an emergency measure but should be instituted only after a period of conservative treatment and long deliberation.

The pathologic picture, the anatomic variations, the virulence of the organism and the resistance of the patient are factors which must be considered. Such infections as erysipelas, lobar pneumonia, endocarditis, empyema and tonsillitis may be primary, concomitant with or sequential to suppuration of the temporal bone and may produce virulent septic symptoms which can be readily misinterpreted as phlebitis and thrombosis of the lateral sinus.

Bacteriology—The early diagnosis of thrombosis of the lateral sinus or of the jugular bulb, before the manifest and evident clinical picture has appeared, and consequent early operation will contribute greatly to diminish the morbidity, the metastases and the mortality from the disease. It is the opinion of J. L. Goldman⁷⁷ that adequate and complete studies of the blood culture with their proper interpretation will help to achieve this end to a gratifying degree.

Bacteremia is the most constant clinical feature in cases of thrombosis of the lateral sinus. Accordingly, recognition of the bacteremia is an important finding for the diagnosis and management of otitic sepsis The microorganism usually isolated from the blood stream is Streptococcus hemolyticus It was recovered from 957 per cent of Goldman's cases of proved bacteremia associated with otitic sepsis and, therefore, thrombosis of the lateral sinus is essentially a disease caused by this organism The demonstration of the invasion of the blood stream is dependent upon the methods used in taking and cultivating the blood Attention is directed to consideration of the number of microorganisms cultured and their growth in fluid mediums alone When all other clinical possibilities have been eliminated, the finding of Streptococcus hemolyticus in a case of suspected otitis sepsis, speaks for lateral sinus or jugular bulb thrombosis This is particularly important in the diagnosis of septicemia when there is a vague office history with inconclusive clinical findings, in the management of proved otitis sepsis and in the differential diagnosis of conditions simulating otitic sepsis. In Goldman's experience, infections confined to the middle ear and mastoid bone have not been associated with bacterenna Clinically significant bacteremia should be differentiated from clinically insignificant bacteremia.

The infrequency of the occurrence of Bacillus proteus in otogenic infections

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and the high mortality make it of sufficient interest to justify the report of a case by B. G. Gerzog. Such infections are usually found in chronically infected ears and may be considered a secondary rather than a primary invader. The organism causes slow, progressive, putrefactive necrosis with extreme toxemia. The organism seems to have an affinity for vascular walls, since 50 per cent of the patients have necrosed sinuses and 1 patient died of pulmonary hemorrhage.

The case reported was of a 12-yearold girl, who had a mastoidectomy 4 years previous to her complaint of mastoid pain, frontal headache, left hemicrania and intermittent chills and fever The left lateral sinus was exposed and found filled with a foul-smelling pus The internal jugular vein was ligated When B. proteus was discovered in pus from the mastoid and blood, a stock bacteriophage was given intravenously for 7 days (1 cc in 1:10 dilution being given and the 1 cc. of the undiluted serum every 45 minutes until 40 cc had been administered) The dose was varied from day to day according to the patient's reaction, which was characterized by severe chills and extremely high temperatures up to 107° F. (416° Blood cultures were taken at 48hour intervals The author feels that the successful outcome of the case is attributable to the employment of the bacteriophage

Treatment — There is no evidence from either the correspondence or a survey of recent literature that the type of treatment influences the mortality. This seems to be affected more by the age of the patient, the virulence of the infection and the presence or absence of complications.

Despite the growing number of authors in the literature who oppose operative intervention on the jugular vein

in the treatment of thrombosis of the lateral sinus, the survey shows that exposure of the sinus with ligation of the jugular vein is still the method of choice of a preponderant number of otologists. This surgical procedure is accompanied with transfusions and the administration of specific serums, tonics and drugs, such as sulfanilamide.

There is evident disagreement about the wisdom of attacking the jugular vein and the efficacy and effect of transfusions and a great deal of discussion about the rôle that sulfanilamide is to play in the treatment of this condition. These controversies and discussions emphasize that much is yet to be learned about this serious complication of mastoid disease.

Since the experience of the individual otologist with thrombosis of the lateral sinus is necessarily limited by the rarity of the condition, the only way by which additional knowledge and better management are to be acquired is by the collective experience of the members of the medical profession

This fact leads to a plea to the individual physician and surgeon to make careful observations and complete and accurate records. This survey furnishes adequate proof of the need for such records. Almost half of the persons who replied to the questionnaire could not give exact information, either because their records were not in such shape that the information was easily available

The importance of all possible knowledge of a condition in which the mortality is approximately one-third is obvious. The individual otologist can hope for improved results only if the collective experience and wisdom of the members of the profession is available to him.

A review of the literature of bilateral thrombophlebitis is presented by M T

Smith.⁷² The case reported by the author was one in which there was streptococcus hemolyticus in the blood stream. Operation was followed by recovery. Smith believes that bilateral operation on the venous sinuses and

ligation of the jugular veins may be the means of saving the lives of many patients, provided a sufficient time is allowed to elapse between operations to allow establishment of collateral circulation.

DISEASES OF THE PHARYNX

By HANS BRUNNER, M D.

TONSILS

Pathology—Starry¹⁰³ presents a very important contribution to the pathology of the faucial tonsils. In the routine histological examination of 8516 additional pairs of tonsils, 7 cases of tonsillar tuberculosis, 5 cases of syphilis of the tonsils, 4 cases of tumors of the tonsils and 1 case of trichina were found. Compared with a previous serial examination there was a marked decrease in the incidence of tonsillar tuberculosis The common pathological lesion in syphilis was an epithehoid proliferation with many giant New blood vessel formation was present in all and served to differentiate the lesion from a diffuse tuberculosis of the tonsils. It is somewhat surprising that Starry found many spirochetes within the syphilitic tonsils, masmuch as the cases reported represent mainly a late stage of acquired syphilis. Since in that stage the spirocheta pallida is not present, at least in lymphoid tissue, the question arises whether or not the spirochetes seen by Starry were actually the spirocheta pallida The trichina was found only in the muscle tissue found in and attached to the capsule Among the 4 tumor cases 1 was a lymphosarcoma in a boy aged 16, the second a squamous cell carcinoma in an adult and the last 2 were papillomas in adults. It must be remembered that there are cases of carcinoma of tonsils which for a long period

of time may fail to yield clinical symptoms and which can be discovered only by a routine histological examination of the tonsils as shown long ago by Urbantschitsch.

In the prodromal stage of measles many multinucleated giant cells are found scattered throughout the tonsils. The germ centers show the most marked reaction. Occasionally small areas of focal necrosis could be seen also These areas contained a few polynuclear leukocytes along with cell fragments There was considerable edema and congestion

The pathology of chronic tonsillitis was discussed by Diamant,84 Heyer,95 Frank and Blahd 88 Frank and Blahd88 found, in 2 of 30 dogs, after intratonsillar injection of virulent beta hemolytic streptococci, that acute endocarditis developed. The hemolytic streptococci used had previously produced endocarditis in 40 per cent of a series of 25 dogs Endocarditis did not develop in any of 15 tonsillectomized dogs after repeated introduction of the same organism into the tonsillar bed and parapharyngeal region. Furthermore, repeated blood cultures of the control dogs remained sterile It is likely that the tonsils played a rôle in the development of bacteremia and endocarditis in these experiments. The authors believe that these studies present experimental confirmation of the favorable clinical results in respect to

prophylactic tonsillectomy for endocarditis. Diamant⁸⁴ studied the pathologic connections between tonsils and arthritis. He found a shift to the left of the blood count only in one-third of 50 patients suffering from joint diseases and even in these cases the shift to the left was only transitory. Operations on tonsils had no effect whatever on the blood count.

Hever⁹⁵ repeated the work of V. Schmidt which was published in 1926. According to Schmidt, a slight massage of normal tonsils produces a transitory lymphopenia, provided that the individual examined has not not eaten before. However, he could not confirm the findings of Schmidt, namely, that slight massage of chronic inflamed tonsils produces a transitory leukocytosis; he rather found different results in these circumstances. Consequently, the text of Schmidt is valuable for the diagnosis of a chronic tonsillitis only, when it is positive, namely, when it produces a transitory leukocytosis.

Gerrie⁹² describes the findings in a girl 8 years old with many malformations. There was microtia, polydactylism and a congenital absence of 1 tonsil and the anterior pillar.

Tumors — The surprising latency of certain carcinomas of the tonsils for a long period of time was mentioned by Evans and Odoni, 86 who describe a case of a polyp of the tonsil. The polyp was composed of a connective tissue stroma which was well vascularized and covered by a stratified squamous epithelium layer. The vascular spaces throughout the tumor were numerous and large. There was considerable round cell infiltration and some lymphoid nodulehke structures were scattered throughout the specimen.

Surgery — Israel⁹⁸ expresses the thought that no form of ring-guarded

instrument could ever be as conservative of muscle tissue and as protective to blood vessels as a delicate, careful dissection, which he describes in detail. Although THE REVIEWER favors the dissection even in children, he scarcely believes that the statement of Israel can be generally accepted. Niedelman⁹⁹ recommends electrocoagulation of the tonsils and emphasizes that the method is safe and efficient when surgical removal of the tonsils is contraindicated. As far as the dangers of tonsillectomy are concerned, Frenckner,89 on the basis of experimental investigations and theoretical calculations, considers it impossible that neither dangerous nor fatal venous emboli could be induced in connection with local anesthesia for tonsillectomy.

Baer⁸⁰ found that vitamins C and B_1 diminish the postoperative pains after tonsillectomy and accelerate the epidermization of the wounds. He, therefore, recommends that *vitamins* C and B_1 be administered routinely after tonsillectomy

Oser¹⁰⁰ studied the occurrence of postoperative hemorrhages after tonsillectomies and adenoidectomies. He found that the danger of postoperative hemorrhage is greater after tonsillectomies performed under local analgesia than those under general anesthesia Furthermore, he observed postoperative hemorrhages 4 times more often in adults than in children In dealing with postoperative hemorrhages the question arises as to whether or not the saliva has an influence upon the blood coagulation \olker,104 who studied this problem exhaustively, found that saliva does hasten it. An aqueous solution of salivary protems exhibited activity similar to that of unadulterated saliva Evidence has been presented which indicates that saliva accelerates blood coagulation by neutralizing the anticoagulant in the blood

Inasmuch as dilution of blood resulted in diminished clotting time, it is suggested that the dilution of the antithrombin is responsible for at least a portion of the reduction in coagulation time

Eigler⁸⁵ examined the amylolytic effect of the saliva before and after tonsillectomy in 16 patients. There were no marked differences from the normal conditions until 9 days after the operation On the twelfth and thirteenth day after the operation, however, a marked decrease of the amylolytic effect occurred, which is supposed to be due to the lack of lymphocytes emigrating from the tonsils into the saliva.

Parapharyngeal Abscess

The importance and dangers of these abscesses cannot be emphasized strongly enough, as shown by the case of Witchell¹⁰⁷ in a man aged 28, who became ill 7 days before with a sore throat and high fever which subsided When seen by the author he again had fever fluctuating between 102° and 1036° F (39° and 398° C) Thirteen days after the onset of the sore throat, tenderness developed over the middle of the left sternocleidomastoid muscle. The left tonsil protruded slightly more into the pharynx than the right tonsil was a marked and increasing leukocyto-Sulfanilamide was administered, and 15 days after the onset of sore throat a retrotonsillar abscess was drained into the pharynx Despite this operation, no decrease of fever occurred, so that 18 days after the onset the vessel sheath was exposed. There were no pus and no thrombus in the jugular vein The operation did not diminish the fever, and 28 days after the onset verbal aphasia, choked discs and high fever were noticed. The neurologic examination confirmed the diagnosis of a meningitis,

although in the cerebrospinal fluid there was a trace of globulin and only 300 cells, mostly polynuclear leukocytes. The patient died and upon autopsy a localized purulent meningoencephalitis of the left temporo-parieto-frontal lobe, cortical abscesses in the cerebellum, empyema of the left transverse, sigmoid, cavernous and superior petrosal sinuses and an empyema of the sphenoid sinus were found.

THE REVIEWER believes that in this case the drainage of the parapharyngeal space by an external approach was strictly indicated. The exposure of the vessel sheath was not sufficient, since in these cases the inflammation and the suppuration of the parapharyngeal space occur earlier and more frequently than the formation of a thrombus in the jugular vein. This statement should not express the idea that the formation of a thrombus in the jugular vein is a rather rare occurrence in such cases. The case of Gilmore^{9,3} would prove the contrary. In a girl, 41/2 years old, an adenotonsillectomy was performed at the age of 3 years. In the pharynx a fluctuant mass was noted on the right side extending the length of the posterior pillar. The fluctuant area was incised and a small amount of pus liberated. The incision was followed by symptoms of septicemia Recovery occurred after external operation and dissection of the thrombosed jugular vein. In order to avoid surgical failures both operations should be performed in these cases principally: The drainage of the parapharyngeal space and the exposure of the vessel sheath.

Waldapfel¹⁰⁶ describes as a morbid entity the parapharyngeal abscesses of the lymph nodes after tonsillitis, which disease, as a rule, comes under the surgical nomenclature of "lymphoma colli." The disease is characterized by the fol-

lowing clinical and pathological findings: The patients become ill with an acute tonsillitis, which subsides after a time. In from 1 to 4 weeks after the tonsillitis. a swelling appears on one side of the neck. The swelling varies in size, sometimes it is as large as an apple; it is firm, slightly tender, immovable and there is no fluctuation. There is no acute tonsillitis, but the tonsils as well as the lateral wall of the pharynx are bulged into the pharynx There is slight fever and a not very marked leukocytosis. At first, the patients do not complain of pain, but later there occur pain radiating into the ears, trismus due to inflammation around the mandibular joint, pain on swallowing due to an inflammation of the pharyngeal muscles and pain on moving the head due to an inflammation of the retropharyngeal space.

The pathology of these cases is ob-There is a suppuration of the cervical lymph nodes with a sequel of inflammation of the connective tissue of the parapharyngeal space. Consequently, it is unjustified to consider the connective tissue of the parapharyngeal space as the only pathway for a progressive phlegmon spreading either into the skull or into the mediastinum. Under certain circumstances, which of course are not entirely understood, the connective tissue of the parapharyngeal space reacts to an infection, by the development of firm adhesions which are intended to restrict the infection and encapsulate the suppuration The disease may run a very inconspicuous course for a certain period of time Spontaneous perforation of the abscess into the pharynx rarely occurs Consequently, if the abscess is not drained at the time, it may rupture into the tissues of the neck with the possible production of mediastinitis, meningitis, septicemia, etc Warning symptoms consist of edema of the larynx, fever, chill or enlargement of the vertebro-laryngeal space in the lateral x-ray of the cervical area. The treatment is simple, consisting of *incision* and *drainage* of the abscess cavity.

Chronic Inflammations of the Pharynx

Lupus—Brueggermann⁸² reports exhaustively about lupus in otolaryngology. From the pathological point of view lupus of the mucous membrane is the manifestation of a particularly chronic course of a hematogenous type of tuberculosis. From the clinical point of view, lupus has the following characteristics: (a) A relatively insignificant development of symptoms; (b) a propensity for formation of scars; (c) by spreading from the nose to the pharynx and lar-The tendency for development of scars indicates a high degree of immunity of the organism, while the exudative-necrotic changes in tuberculosis of the mucous membrane accompanying a tuberculosis of the lungs indicate a low state of immunity of the body However, the development and the course of the lupus also depend upon the immunity of the affected organ itself. In general, it is not true that lupus of the mucous membrane is without danger, as was formerly believed, because of the experience with the lupus of the skin in which the immunity of the body is generally better than in lupus of the mucous membrane Admittedly, lupus of the larynx is dangerous even for life, particularly when the larvnx and mouth or larvnx and pharynx are simultaneously affected Also, the prognosis of lupus of the mucous membrane is poor, masmuch as recurrence may occur on the same place where the lupus was formerly healed.

In the mouth, the soft and hard palate, on the inside of the cheeks, and on the mucous membrane of the lips, lupus sets in with a node covered by normal mucous membrane. Often there are fissures at the angle of the mouth which do not respond to any treatment. Lupus of the tongue is rare. If lupus of the pharynx heals, scars develop which may obliterate the entire isthmus between the oro- and the nasopharynx.

In order to differentiate lupus from carcinoma, a biopsy must be performed Mistakes are possible even with biopsies, consequently repeated biopsies are required One has to bear in mind that the development of a carcinoma on the base of a lupus of the skin is much more frequent than on the base of a carcinoma of the mucous membrane

It is sometimes difficult to differentiate between lupus and rhinoscleroma, although the latter spreads much more rapidly and produces more connective tissue than does lupus

Treatment — The treatment is both general and local The general treatment consists of heliotherapy and a salt-free diet. Local treatment depends upon the immunity of the body. When there is a strong immunity of the body, the excision of the lupus and the cauterization with lactic acid, trichloracetic acid, 10 per cent pyrogallous vaseline or the freezing with a mixture of carbon dioxide snow and acetone or, finally, diathermy, are to be considered. The local application of x-rays has not proved successful. The local application of large doses of radium has greater merit. There is not the danger of provoking the development of a carcinoma by applications of x-rays or radium to a lesion of lupus of the mucous membrane, such as frequently occurs in cases of lupus of the skin

Rhinoscleroma — Gadomski⁹¹ presents an excellent survey regarding the pathology and symptomatology of rhino-

scleroma and describes the following case:

A girl, aged 26, who was born in the southern part of Poland and lived there until the age of 18, before she came to this country. She had marked changes in the nose. In the throat the anterior and posterior pillars, the uvula and the soft palate were matted together with the posterior wall of the pharynx, obliterating the lateral pharyngeal recess and in part the nasopharynx. The tonsils were almost completely destroyed. The hypopharynx was narrowed markedly, it was granular and red and covered by thick mucopus Injections of autogenous vaccine were administered with success.

Closure of Nasopharynx—In a case with complete closure of the nasopharynx following fever, Goodyear⁹⁴ has tried the following procedure. A number 4 sinus dilator was passed through the nose into the pharyngeal wall. The sound was pressed firmly into the adherent area and the tissue was cut horizontally down to the point of the instrument. The sound was then moved about and the incision continued as far laterally as possible. This procedure is not entirely new, it yields, however, only occasional permanent results.

Inflammation of the Tongue

Waldapfel¹⁰⁵ stresses the importance of the acute infection of the circumvallate papilla He describes a case of an infection of a circumvallate papilla and its related serous glands with retention and abscess formation. There was extreme tenderness of the tongue, which was swollen but movable, while the floor of the mouth was free from infection. The base of the tongue was not involved and there was no edema of the larynx, but there was slight fever. The prognosis of these cases is generally good. The treatment consists of conservative measures. such as heat and antiphlogistic treatment.

Ipolyi⁹⁷ observed, in a man, aged 50, a *Plant-Vincent's infection* at the base of

the tongue spreading over the epiglottic. Recovery ensued after the local application of *trypaflavin*.

Tumors

General Considerations—Binkley81 discusses the important question as to how to make certain of the diagnosis in lymphomatous diseases of the neck. Surgical excision of an involved lymph node is the method of choice for obtaining biopsy material For certain patients it is necessary to repeat the procedure during the course of the disease in order to establish a definite diagnosis. In this group of diseases, needle puncture and aspiration are reserved for patients in whom there are no accessible diseased lymph nodes suitable for excision and for whom removal of a wedge is not Smears of aspirated material feasible are supplemented, when possible, by additional biopsy material obtained during the course of the disease. (The RE-VIEWER Wishes to recall that several years ago he recommended, in patients in whom there are no acessible diseased lymph nodes suitable for excision, that the contents of the crypts of the faucial tonsils be examined or one should perform a puncture of the tonsils, provided, of course, that the tonsils had not been previously removed)

In a very interesting paper, Zwingli¹⁰⁸ reports the examination of 1349 biopsies taken from carcinomas of the upper respiratory and digestive tracts. In grouping these cases the author follows the work of Duval and Lacassagne, who have divided these malignancies into:

(a) Epithelioma indifferencie (tumors which are entirely immature and do not show any differentiation); (b) type intermediaire (tumors with a hinted differentiation); (c) epithelioma epidermoides (tumors with a definite differentiation). The differentiation in the

latter tumors may develop either into the structure of the skin (skin type) or into the structure of the mucous membrane (mucous membrane type) or may finally develop into a structure which resembles partly the skin, partly the mucous membrane (mixed type).

In continuation of his studies, Zwingli examined the radioresistance of these tumors, emphasizing the fact that the lack of sensitiveness of a tumor against rays is not identical with its curability. A tumor may be very radioresistant, nevertheless it may produce metastases and even kill the patient. Bearing in mind this definition, he found that the mucous membrane type is much more sensitive than is the skin type, the localization of the tumor being of less importance. Nevertheless, it was found that squamous cell carcinomas of the pharynx and larynx of the skin type as well as of the mucous membrane type are more sensitive than tumors of the same type when they are located in the mobile part of the tongue.

Tongue—In a girl, aged 13, Smith¹⁰² observed a tumor at the base of the tongue The symptoms due to that tumor were a choking sensation and difficult breathing, especially after strenuous exercise or excitement. A biopsy taken from the tumor revealed normal thyroid tissue, proving the diagnosis of a lingual thyroid Administration of iodine improved the condition Frenckner⁹⁰ observed 16 cases of tumors of the base of the tongue, among them 7 being lingual goiters In 5 of these 7 cases, operation was performed, I case being followed by hypothyroidism That case was a woman. 35 years old, with frequent inflammations of the lingual goiter Consequently, the entire lingual goiter had to be removed by the endoral approach After the operation hypothyroidism developed, which was controlled by the administration of thyroid. The hypothyroidism developed despite the fact that there was a palpable thyroid in the neck.

Palate—Hill⁹⁶ deals with mixed tumors of the hard palate. While these tumors are usually diagnosed without difficulty, there may be some confusion with epithelial or mucous cysts, the diagnosis depending upon microscopic findings. Palatal mixed tumors are po-

tumor use of radium needles, she developed metastases to the left hilum and later of the liver and spine.

Pharynx — Fox⁸⁷ reports on mixed tumors of the salivary gland type observed in the pharynx, although in his own cases the tumors were not actually in or connected with the glands. They were fully encapsulated and wholly apart from the salivary glands, apparently

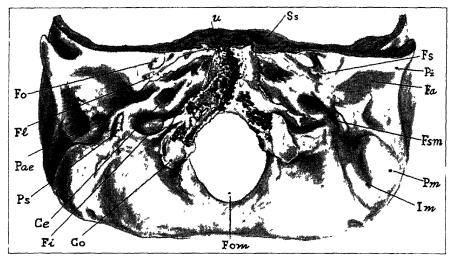


Fig 26—Base of the skull. Fom, Foramen occipitale magnum. Co, condulus occipitalis, Fi, foramen jugulare, Cc, canalis caroticus, Ps, processus styloideus, Pac, porus acusticus externus Fi, foramen lacerum, Fo, foramen ovale, U, ulceration on the base of the skull, Ss, sinus splenoidalis, Fs, foramen spinosum, Ps, processus zygomaticus, Fa, fovea articularis, Fsm, foramen stylomastoideum, Pm, processus mastoideus, Im, incisura mastoidea (Brunner Arch Otolaryng)

tentially malignant. While carcinomatous changes are far less common than in parotid tumors, the histology is similar and mitotic figures may be found.

Rare tumors are described by Robb and Michels¹⁰¹ and Arons.⁷⁹ Robb and Michels¹⁰¹ saw a primary squamous cell carcinoma of the uvula. The symptoms were pain, difficulty in swallowing, dryness, hoarseness, and a tickling sensation in the throat. In differentiated infiltrating types of the neoplasms, early excision offers a better prognosis than irradiation therapy alone. The case of Arons⁷⁹ was a melanocarcinoma of the hard palate in a woman 52 years of age. Despite x-ray therapy and the intra-

having developed from cells that were detached during the embryonic stage. The tumors occupied a space medial to the investing layer of the cervical fascia, anterior to the prevertebral and posterior to the pretracheal fascia.

The symptoms are quite typical There is a swelling just below the angle of the lower jaw, fullness in the region of the tonsils, inconvenience, but no distress, when swallowing, no inflammation of skin, bulging of the lateral pharyngeal wall, invasion of soft palate and bulging downward and medial in continuation with the prominence of the pharynx. Biopsy of tissue removed from the growth itself is unnecessary because the

appearance of the tumor is so distinctive that it should be recognized. Removal of a specimen for biopsy destroys the integrity of the capsule and causes scar tissue to form between the capsule and surrounding structures. Removal of a cervical node for biopsy is contraindicated, inasmuch as the nodes show no tumor cells and the resultant scar tissue is so great that removal of the fully

Brunner⁸³ studied the extension of a carcinoma of the epipharynx along the base of the skull. The tumor had grown along the clivus backward as far as the occipital great foramen, where it had partly destroyed the articulation between the atlas and the base of the skull. The lamina interna of the clivus was intact, although the tumor had invaded the greatest part of the clivus. A roentgeno-

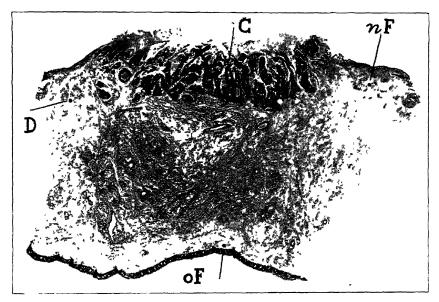


Fig. 27—Carcinoma by contact (C) on the nasal surface of the soft palate (nF), oF, oral surface of the soft palate, D, layer of mixed glands, staining with hematoxylin-eosin (Brunner Arch Otolaryng)

encapsulated tumor is impossible Complete excision of tumor can and should be accomplished through an intrapharyngeal incision after ligation of the external carotid artery. There will be no recurrence if all tumor tissue is removed.

The advice given by Fox concerning biopsy should not be generalized. Unquestionably, there is no reason to remove a piece of an encapsulated tumor for biopsy, the complete removal of the tumor serving for diagnosis and treatment. However, there are other states in which tumors are without a capsule. In such cases no treatment of any kind should be indicated without biopsy.

gram made of the macerated specimen revealed normal diploetic tips of the petrous bones The bone of the clivus produced a fine shadow, signifying a thin but normal bone Hence, in comparison with the specimen itself, the roentgenogram gave a far from exact impression of the extension of the destruction within the clivus. Under these circumstances, Brunner believes that one cannot expect an exact picture of the base of the skull when the roentgenogram is made during A normal roentgenogram of the hase of the skull in a case of carcinoma of the epipharynx, therefore, does not prove very much. In the same case

Brunner found a carcinoma on the nasal surface of the soft palate which is supposed to be developed by contact with the tumor in the epipharynx. The tumor of the soft palate had already broken into the lymph vessels of the soft palate. Consequently, metastases could be produced by the tumor in the epipharynx as well as by the tumor of the soft palate.

It is obvious that this tumor of the soft palate may restrict the motility of

the soft palate. As it is well known, the restriction of the motility of the soft palate belongs to Trotter's triad, which is characteristic of malignant tumors of the epipharynx and is explained by Trotter by a carcinomatous infiltration of the muscles of the soft palate. The case of Brunner proves that this symptom may be also produced by a carcinoma due to contact with the nasal surface of the soft palate.

RHINOLOGY

By O E. VAN ALYEA, M D.

The Common Cold

Etiology — The primary etiological agent of the common cold is, in all probability, a filterable virus. Whether it is a single strain or any one of several distinct strains has not yet been determined. It is fairly certain, however, that the cold virus is not identical with the virus of human influenza.

Kneeland¹⁰⁹ calls attention to the nasopharying as a habitat of microorganisms of varying degrees of virulence. One of the principal dangers of an acute common cold is that it may activate these potentially pathogenic organisms so that (a) they increase the severity and add to the suppurative complications of the cold, and (b) they become imbued with a new capacity to spread to and infect other people.

Prophylaxis—Three modes of prophylactic attack are theoretically available General measures, local measures, and specific measures Good nutrition, general hygiene and adequate vitamin intake are advocated as a possible aid in the prevention of colds. Local measures, such as removal of foci in the upper respiratory tract and correcting anatomical abnormalities, are undoubtedly of benefit.

It would obviously be desirable to create an immunity against the cold virus itself, but to date all attempts have been unsuccessful. The next prophylactic aim, therefore, is to try to increase the individual's resistance to the secondary bacterial invaders which are responsible for the severity and complications of the common cold. This seems possible in certain individuals, viz, those with a tendency to recurrent sinusitis and bronchitis and children who each winter are ill for a considerable period with upper respiratory infections complicated with fever or otitis media.

Jarvis¹¹⁰ recognizes 12 varieties of the common cold and suggests treatment applicable to each type. The 12 varieties are: (1) The open window cold (2) The dusty trade cold (3) The perspiration cold. (4) The sugar cold (5) The chemical vapor cold (6) The fruit and vegetable cold (7) The citric acid cold. (8) The postfestival cold (9) Vasomotor rhinitus (10) The starch cold (11) Influenza cold (12) The drug cold.

The Open Window Cold—For those individuals who spend their daytimes indoors the night air of northern win-

ters is too cold for the tissues within the nose. This especially applies to those who suffer from cold hands and feet, who cannot stand draughts. These individuals, as a rule, present characteristics of a dominant parasympathetic division of the autonomic nervous system. They usually have a subnormal temperature, slow pulse and low systolic blood pressure. An aid in the treatment of the open window cold is *insulin* injected subcutaneously in 3-unit doses daily for 3 days.

The Perspiration Cold—The perspiration cold is due to excessive sweating following exercise. The biochemical balance of the body is upset with the pouring out of perspiration which depletes it of mineral salts, especially sodium chloride. A watery masal discharge develops. Patients respond quickly with a cessation of discharge when given a teaspoonful of table salt in water.

The Dust Cold—The dusty trade and chemical vapor colds occur in those whose nasal mucosa becomes irritated when they inhale dust (granite cutters) or the fumes of fresh paint

The Fruit and Vegetable Cold—This happens often with individuals on a reducing thet. By eating only fruits and vegetables an excess of potassium and iodine is present in the body which disturbs the sodium potassium and chlorine-iodine balance. A watery nasal discharge results A change of diet and insulin injections will effect an early cure

Citric Acid Cold—Symptoms of a cold may be produced by the intake of large quantities of the juice from oranges or other citrous fruits. Immediate relief is noted when these are eliminated from the diet

The Postfestival Cold—This may occur when the intake of food is greater than the metabolic ability of the indi-

vidual is able to cope with. He should be given an enema or cathartic with a reduction of food intake.

Vasomotor Rhinitis—This is due to a block in cell oxidation similar to that of sugar, starch and citrous fruits. Prescribe dilute hydrochloric acid, 5 m in a glass of water on arising, at 10 A. M., 3 P. M. and bedtime, to serve as an oxidizing catalyst. Also give Amend's solution 1 or more times daily. He may also be given 1 tablespoonful of mazola oil (corn oil) before each meal.

Starch and Sugar Colds—Certain individuals have a low tolerance for sugar or starches and this may cause them to suffer a block in the body process of cell oxidation when the intake of carbohydrates becomes excessive ¹¹¹ This may be accompanied by a chain of symptoms, such as: Constant fatigue; pains, inability to concentrate, mental depression, headaches, vertigo, shortness of breath, an easily tiring voice and insomnia

This syndrome may be followed by a variety of clinical conditions involving the nose and throat. A watery mucopurulent discharge is present; the turbinates are enlarged and the sinuses are dark on transillumination. The treatment recommended for this condition is.

- (a) Restrict intake of food which may cause the oxidation block Substitute rye bread, commeal and oatmeal foods for wheat, honey for sugar, apple and grape juice for the citric acid juices (b) Oxidizing catalysts or activators
- are given to overcome the block in cell oxidation. These consist of daily injections of 3 units of plain *insulin* and 3 drops of *Amend's solution* in a glass of water 20 minutes before meals

Salt for Colds—A teaspoonful of table salt, taken in a glass of water, is likely to do more to stop a cold than alkaline drinks, Goodyear¹¹² believes. It is not generally realized that bacteria re-

quire an alkaline medium for growth. Therefore, colds are not likely to subside when the patient consumes large quantities of orange juice, soda and alkaline drinks. Nasal and body secretions are normally slightly acid and offer the greatest resistance to bacterial growths

Cold Vaccines—In their controlled study of the value of "cold vaccines"



Fig 28—The lateral head-low position Ephedrine in saline solution is instilled into both nasal chambers, the 2 sides being treated simultaneously. All the sinal ostiums of both sides are flooded by the solution. In adults this posture may be used for the displacement of iodized oil into the sinuses by the Proetz method. (Parkinson, J.A.M.A.)

the Hausers¹¹³ gave cold vaccine subcutaneously to the first 10 persons, intradermally to the next 10 and placebos to the following 10. This cycle was repeated until there were 100 persons in each group. After this number was reached the vaccine was given subcutaneously to the next 100 who presented themselves at the clinic for treatment The first injections were given during the third week in October and the last one by the middle of December During the last 2 weeks in May each student who had received the injections was interviewed, provided he had completed the series Data were obtained from 188 persons who had received the vaccine

subcutaneously, from 95 who had received it intradermally and 86 to whom placebos had been given. Of the persons who had received the vaccine subcutaneously, 74 per cent said that they had had fewer colds, 6 per cent that they had had no colds at all, 18 per cent that they had the same number as during the preceding year and 2 per cent that they had more colds. Of those who had received the vaccine intradermally. 526 per cent reported that they had had fewer colds, 116 per cent that they had no colds at all, 326 per cent that they had the same number as before and 3.2 per cent that they had more colds Among those who had received placebos, 605 per cent reported that they had had fewer colds, 5.8 per cent that they had no colds at all, 314 per cent that they had the same number as the last year and 2.3 per cent that they had more colds More than 90 per cent of all the subjects expressed a desire to be similarly treated the following year.

Treatment—Local Therapy—Parkinson¹¹⁴ again calls attention to his lateral head-low posture in treatment of upper respiratory infections. Solutions of ephedrine, 1 per cent or less, in normal saline, are advocated as a safe decongestant in all stages of the infection Patients of all ages from infancy to old age may be thus treated Adults lie on one side on a couch with the lower shoulder supported by 1 or 2 pillows Then, when the head is bent downward to a dependent position all the ostia of both groups of sinuses are available to fluid instilled into the nose and can be reached by treatment that is free of trauma Infants and small children may be held sidewise across the lap while the head is held in a laterally flexed position by pressure of the hand from above.

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Parkinson states: "With all the variations of intranasal structure a few things can be counted on as unvarying, and one of these is that all the sinal ostiums are in the upper half of the nasal fossae." With the head inverted they are in the lower half and are accessible to fluid and gravity. A dropperful of the solution is instilled into each nostril and the position is held for from 3 to 5 minutes. The ephedrine is thus enabled to exert its shrinking effect in the upper meatuses and about all the ostia. During this time, breathing through the mouth will prevent the fluid from being drawn into the pharynx The patient's head is finally rotated to face downward, which allows the fluid to be expelled from the nose.

Oily Preparations — The growing use of oily preparations, both as a source of vitamins and in the treatment of respiratory and gastrointestinal diseases. contributes to the increasing frequency of lipoid pneumonia in infancy and childhood. According to Wolman, 115 infants should be fed cod-liver oil only when awake and held in a semierect or sitting position Oily nose drops in the first 2 vears of life are potentially dangerous; aqueous solutions for intranasal medication being preferable Parents and nurses should be warned against the forcing of cod-liver oil or other oils when the youngster refuses and resists. The blocking of a child's nostrils in order to make him swallow must be absolutely forbidden. Newborn or premature infants and all babies who vonit should be given vitamin concentrates rather than the larger doses of crude cod-liver oil In the feeding of oils and similar substances to weak or debilitated patients, especially to neurologic patients, the greatest forethought and precautionary care should be exercised; that is, aspiration should be prevented at any cost.

General Therapy—During the acute stage of rhinitis or sinusitis, Shea¹¹⁶ believes that the administration of a prescribed mixture may be of value and a prescription may be based on 1 of the following substances: (a) Codeine or morphine sulfate may be used for the relief of pain or as a sedation to arrest a cough. The use of Dover's powders,



Fig 29—Infants and small children are best held over one's lap (Parkinson J A M A)

once very popular, is losing favor because of the frequency of nausea. (b) Monobromated camphor is an antispasmodic Quinine is preferred by some physicians for this rôle (c) Caffeine in the form of a citrate relieves the headache and as a stimulant neutralizes the depressant action of the saliculates (d) Salicylates form the principal part of the prescription Today acetylsalicylic acid is popular and inexpensive. (e) Iodine has long been one of the best alteratives of materia medica Five minims (0.3 cc) of tincture of 10dine U S. P in 2 ounces (60 cc.) of water acts locally and replaces a gargle In the stomach it acts as a functional stimulant and after its absorption increases the discharge of the sinuses and nasal membranes. To maintain shrinkage of the nasal tissues one may administer one-eighth grain (0 008 Gm.) of *ephedrine hypdrochloride* by mouth with a corresponding dose of soluble *phenobarbital*. This combination may be prescribed as a follow-up treatment until the next office visit.



Fig 30—Completion of treatment by turning the child face down, permitting the nasal contents to escape from the nostrils. With this technic none of the solution at any time enters the throat (Parkinson, J. A. M. A.)

Nasal Allergy

Kern and Schenck¹¹⁷ are definitely of the opinion that polypi are in every instance an evidence of an allergic basis and make the statement that "avoidance of, or desensitization with allergens yields clinical results far superior to the old routine of surgical removal alone with its distressingly frequent recurrence of the polyps" They advise against any surgical treatment during the pollinating season and advise removal of polyps only when they are obstructive Their entire emphasis is on the allergic side of the question, minimizing the question of coincident infection and the necessity for surgical intervention.

Reeder¹¹⁸ handles the nasal allergy case with an initial roentgen study of the sinuses. If the x-rays are negative for polyps and examination of the nose is negative, he starts treatment with a diet of acid base foods. Internally he gives hydrochloric acid or nitro-hydrochloric acid at mealtime. Under this régime a very pale mucosa will change to a normal pink in about 3 weeks. After that an alkaline food may be added to the diet each day until recurrence of symptoms. If this procedure fails to control symptoms the eliminating test diet is indicated; if this fails one should start testing for external allergens.

Reuling, in discussing the above paper, says he thinks the common use of soda, citrocarbonate, citrous fruits, and alkaline diets for the prevention and cure of colds has produced alkalosis and a watery, boggy nasal membrane in many cases. He prescribes hydrochloric acid for this condition. He also calls attention to the possibility of vasomotor rhimits with hypothyroidism as a cause of the nasal blockage. Ninety per cent of the allergens, he says, are included in the following. Feathers; fur, wool, orris root, tobacco, chocolate, wheat and milk

Asthma — There is no doubt that many patients with sinus involvement are allergic and should not be operated on According to Ramirez, 119 however, the bronchospastic type of asthma resulting from remote reflex stimuli originating in the nose or the accessory sinuses obviously will not be benefited except by elimination of the local pathologic condition In cases of bronchoedematous asthma in which sensitization has taken place a gross nasal pathologic condition must be corrected surgically if lasting satisfactory relief of symptoms is to be expected; this, of course, must be in addition to proper treatment from

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an allergic standpoint. Grains of pollen embedded in the lining membrane of the antrums and possibly of the other sinuses may in this way be responsible for the continuance of symptoms in highly sensitive persons after the particular pollen has disappeared from the air of the locality. The author believes that there is a definite relation of endocrine dysfunction and vitamin deficiency not only to asthma but to allergy in general. He does not think that any 1 vitamin is solely responsible. Any gland or combination of glands may be an important factor affecting the underlying fundamental mechanism of hypersensitiveness.

Nasal Allergy in Children—Rhinologists must become allergy-minded to arrive at an accurate diagnosis and to obtain better results in the management and treatment of many nasal complaints in children, according to Barnett and Carnahan. To determine nasal allergy in childhood and to determine whether or not the allergy is complicated by infection, physicians need to perform routine examinations of the nasal secretions and the tests are of more clinical value if carried out in the physician's office, where the results may be closely compared to the progress of the patient

Allergic control is vital if associated surgical procedures are to be of benefit Removal of infected tonsils and adenoids may aggravate symptoms in a child with uncontrolled allergy. Disappointment and discouragement will follow nasal treatments and operations on the sinuses or nose if associated allergy is not simultaneously or previously relieved Removal of nasal polyps in the patient with uncontrolled allergy may be followed by prompt recurrence

Piness and Miller¹²¹ see many children who have been treated for repeated "colds," chronic sinusitis, chronic bron-

chitis and recurrent pneumonia, by "cold shots," sinus drainage and adeno-tonsillectomy until a frank, unmistakable attack of bronchial asthma brings a surprised awakening to the fact that the essential cause of the "colds, sinusitis, bronchitis and pneumonia" is allergy. They stress the fact that allergy is a nonsurgical disease of the nose and throat and deplore the present day vogue of tonsillectomy for its cure.

Atrophic Rhinitis

Hargett¹²² believes that atrophic rhinitis is a deficiency of the mucous glands of the nasal epithelium, either because there is an inadequate number of them or because the function of those present is abnormal, or a combination of the two. When the stratum corneum is removed from the skin, the moist layers beneath refuse to submit to drying and exude lymph and fibrin, which coagulates and dries, forming a protective coating, so that the cells below continue their function in a moist state. The author points out that the same reaction occurs in the mucous membrane of the nose. The microorganisms normally inhabiting the nose invade these scabs and produce the typical ozena.

As this condition persists over a long period, a secondary defensive measure begins on the part of the mucous membrane to form a stratum corneum for itself. This process begins at the junction of the skin and mucous membrane at the opening of the nares and gradually extends backward. The condition never extends into the mouth and seldom into the pharynx, with the large and copious salivary glands to keep these parts moist.

The author knows of nothing that will help the condition after cornification has taken place But before cornification develops treatment should resolve itself into trying to lighten the load of the glands present, to restore them to normal function and perhaps to stimulate their proliferation. Operations which reduce the amount of air going through the nose by moving the lateral walls inward ease the burden of the glands, and some cures are effected. Paranasal sinusitis preceding the atrophic rhinitis coincides with the theory of deficiency. As with the other organs of the body, it seems reasonable that condition of the glands might be improved by periods of rest.

This was tried on a group of patients by placing cotton plugs in one or both nostrils. It was found convenient to have the patient place these plugs in the nose at bedtime and remove them the next morning, giving the membrane 8 or more hours of rest Patients soon become accustomed to the mouth breathing necessitated and make no complaints. If the plugs are used while there is active sinus infection the patient immediately feels worse, and this is an indication for simultaneous treatment of the sinus, always being conservative at first. As soon as the sinusitis begins to improve, the plug treatment may be begun, and at this stage the patient will usually remark on the improvement. If the adenoids are infected they should be removed, but it is well to give preoperative douches daily for about a week

Eagle¹²³ and his associates used *estrogens* in the treatment of 14 patients with atrophic rhinitis. Sections of their nasal mucosa were studied before and during or after treatment with regard to specific histologic alterations attributable to the local action of the estrogens. The first biopsy specimen in each case was obtained previous to any treatment and the second one was taken from 27 to 216 days after the first treatments with estrogenic substances were

started No patient complained specifically of deafness or tinnitus. Twenty-two patients started the estrogenic treatment and had the original biopsy but, owing to economic reasons and the distance to the clinic, 8 did not return for the second biopsy. The patients irrigated their noses twice daily with physiologic solution of sodium chloride or 1:10.000 solution of potassium permanganate and 10 minutes later repeated the irrigation to remove the crusts that had been loosened by the earlier washing. The 0.5 cc. of estrogenic substance was sprayed into the nose twice daily, giving each patient the equivalent of 1 cc. or 1000 international units, of estrogen daily. Twenty-one of the 22 patients reported clinical benefit and each wished to continue treatment. A patient with stormy menopausal symptoms stated that she was not improved in the slightest degree Inspection of the nose revealed a definite diminution or complete eradication of crusts in all 14 cases in which the study was completed, and in no instance was the odor, characteristic of the disease, detectable The only changes noticeable in the mucosa were a slight increase in hyperemia and a smoother surface Patients complaining of a burning sensation in the scalp and occipital headache were relieved of these symptoms. The authors are unable to state whether the patients' noses were free of crusts because of the more frequent irrigations or because of the estrogenic therapy. The impression was that the surface epithelium and the subepithelial glandular system contained more mucous cells after treatment than before. It appeared that amounts of squamous and ciliated epithelium and the vascularity, as well as various other features, were not altered No perfectly consistent change in any one direction

existed. Fibrosis was recorded more frequently before than after treatment.

Nasal Blockade

Lillie and Simonton¹²⁴ state that a common though often overlooked cause for the sensation of blocked nose is "alar collapse." This may be the sole cause of the patient's difficulty in breathing or it may be associated with other anomalies. Before attempting one of the plastic operations to counteract the "alar collapse" the patient should be instructed to breathe before a mirror, using the alar dilator muscles to open the nares. This often effects a cure

Epistaxis

Ionization or iontopheresis such as has been used in the treatment of hay fever was employed by Beck¹²⁵ in 3 cases of severe nasal bleeding in patients suffering from hypertension. The thick fibrous membrane of coagulative necrosis that immediately forms on the surface of the septum had the effect of sealing in the bleeding points. Permanent relief is brought about by the fibrosis produced by the procedure

Nasal Headache

Mussun¹²⁶ describes headache from the middle turbinate. The patients complain of pain at the nasal side of the orbit which occasionally includes the frontal region and areas farther back It usually lasts several hours but may persist for even weeks or months. He thinks the cause is some factor which produces a local congestion in the anterior portion of the middle turbinate, for examination reveals a marked inflammation of that area. The membrane is dry and there is no discharge. He eliminates as a diagnostic consideration vacuum headache and nasociliary neuralgias, as well as neuralgias of the supraorbital or the sphenopalatine nerve. Cocaine usually relieves the condition and permanent relief may be obtained by the removal of the anterior end of the turbinate.

Sinus Disease

Ethmoid Labyrinth—Van Alyea¹²⁷ reports the anatomic findings in a study of the ethmoid cells in 100 specimens from cadavers. The variations in number of cells present (average of 9), size and arrangement were more marked than is generally supposed. The cells, though apparently a jumble, may readily be sorted into groups and classified according to their areas of drainage in the nose. Significant was the presence of a thickened antral mucosa in 18 per cent of the cases and an associated similar involvement of all infundibular ethmord cells (Fig. 31). In some of these the infection extended to the bulla and in a few a pansinusitis included all cavities on one side of the nose Attention is called to the agger nası cell, present in 89 per cent, often overlooked as an entity in sinal infection with orbital manifestations Supraorbital cells (15 per cent) may become infected and simulate frontal sinus disease. Ethmoid cells commonly drain into grooves and are amenable to treatment by irrigation (Fig. 32)

Diagnosis—The diagnosis of chronic infection of the ethmoid sinuses is one of the difficult problems in rhinology. It is particularly difficult in those low-grade chronic infections of the ethmoid sinuses in which the nasal passages appear normal on one or more examinations and in which any symptoms pointing directly to the sinuses are so slight as to be almost nonexistent and yet in which there is sufficient systemic absorption from the ethmoid infection to cause very definite systemic symptoms.

Shambaugh¹²⁸ divides these cases into 5 groups according to the predominating or presenting symptom:

1. The largest group is that in which the patient's chief complaint was pain or headache. The pain of chronic ethmoiditis may be felt in the cheek, ethmoid region, forehead, parietal region or ear. Like any sinus pain, it is worse following acute head colds and worse on 5. The last group of patients had a fever of unexplained origin as the presenting symptom, which was most interesting because fever is rarely seen in chronic infections of the other sinuses

The procedure that the author uses is briefly as follows The symptoms suggest a possible low-grade chronic ethmoid infection in spite of normal appearing nasal passages on posterior as well

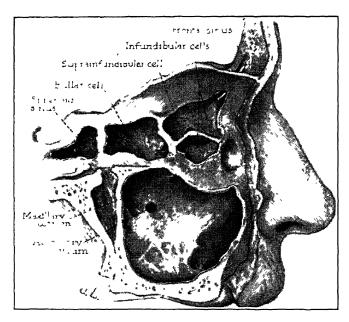


Fig 31—Ethmoid labyrinth composed of 4 cells only. In the specimen illustrated a small frontal sinus drains into an infundibular cell. The lining mucosa of all cavities except the splenoid sinus shows marked thickening. (Van Alyea. Arch. Otolaryng.)

bending forward. These characteristics suggest a sinus origin for the headache and yet the nasal passages appear normal in all respects and there may be no nasal symptoms whatever, and the x-ray examination may be negative for sinus disease.

- 2 In the second group the presenting symptom was an infection in a remote organ, such as iritis, neuritis or arthritis
- 3 The third group of patients complained of chronic and persistent cough for which no cause could be found.
- 4. In the fourth group the chief complaint was frequent head colds

as anterior rhmoscopy A roentgenogram is first taken to rule out infection of the maxillary, frontal or sphenoid sinuses, and if any of these appear infected they are irrigated. With the patient's head hyperextended in the Proetz position, the nasal passages are filled with 0.25 per cent *ephedrine* in physiologic solution of sodium chloride. Alternate suction and release of suction is applied from 4 to 6 times in each nostril, and if frank mucopus is obtained or is blown out into the towel when the patient sits up the diagnosis of ethmoid suppuration is made.

Therapy — Porter¹²⁹ calls attention to the prejudice of the general practitioner and the public to surgical treatment and blames largely the otolaryngologists themselves. This is because of poor surgical technic and lack of good judgment in knowing when to operate.

In acute conditions the primary object is to secure drainage and abatement of inflammatory reaction. He advises rest, moisture and daily shrinkage with weak solution of cocaine followed by warm saline irrigations. Immediate surgery is often necessary in the fulminating type and should be extensive enough to obtain immediate and adequate drainage of all sinuses involved.

Granger¹³⁰ recommends conservatism in the treatment of acute sinusitis. He puts his patients to bed in a room with plenty of moisture in the air. He prescribes liquid diet and suitable medication for fever and pain, the latter occasionally necessitating morphine. Infra-red heat may be applied over the face if it assists in relieving the pain. Some mild vasoconstricting drug may be used sparingly in the nose Many of the medications widely used are actually destructive to the nasal epithelium and favor increased infection by impairing ciliary activity, breaking the first lines of defense. He maintains that all instrumentation should be avoided and even rough handling of cotton tipped applicators which might bruise the acutely inflamed mucosa is contraindicated

Much more can be done for and to the patient in the subacute and chronic stage of sinusitis *Irrigation of the* nasal cavity is a valuable procedure. The solution should be isotonic with blood serum and at body temperature The patient inclines the head forward and breathes evenly through the open mouth while the solution is allowed to flow into 1 nostril and out the other. The solution container should not be more than 1 foot above the patient's head. The patient should not blow the nose for at least 15 minutes after the irrigation.

Suction is of distinct benefit in ethmoid and frontal infection. The suction

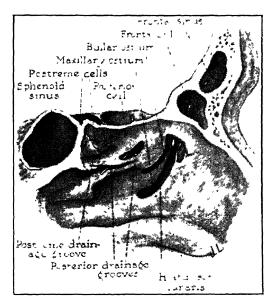


Fig 32—Drainage grooves of the ethmoid cells. The frontal cell in the specimen illustrated has its ostium in the frontal recess anterior to the uncinate process. (Van Alyea Arch Otolaryng.)

should be mild; and applied intermittently only a few times. Injudicious use of too high negative pressure causes bleeding, congestion in the mucosa, and pain, and makes the patient worse instead of better.

The displacement method of sinus treatment is especially valuable in those cases where the viscosity of the muco-purulent material is such that it escapes from the sinus with difficulty, tending to adhere to the walls. Also when a swollen mucosa partially occludes the opening of the sinus.

Fracture of the middle turbinate toward the septum is a procedure that

has been of great benefit in treatment of ethmoid infections. In the subacute condition the secretion is likely to be too thick and tenacious to escape readily from the ethmoid area, especially in those cases wherein the middle turbinate lies very close to the lateral wall of the nose. Under cocaine anesthesia the middle turbinate bone is fractured toward the septum so as to permit a good view of the condition of the tissues underneath. This procedure alone will occasionally suffice to secure adequate drainage with mild suction. It also favors the application of suitable agents to the infected area Fracture of the middle turbinate also aids in the search for the natural opening of the maxillary sinus.

Fox and his associates 134 describe their technic for postural postnasal irrigation in the treatment of subacute residual ethmoiditis following colds. After shrinkage of the nasal membranes the patient is placed on his back with his head down in the Proetz position and the nose is filled with a saline solution A mild suction, while the patient repeats "KKK," stirs up the solution and the nasal membrane is thoroughly cleansed It is doubtful if much solution runs into the sinuses by this technic, although it is possible if the menbrane lining the ostia of the post ethnioid and sphenoid are properly shrunk. This form of treatment is especially indicated in the presence of headache associated with lowgrade suppurative and hyperplastic disease of the ethmoid cells. The number of irrigations required varies with the length of time the condition has been present In the early subacute types 2 to 4 are sufficient, given at 48-hour intervals In 300 cases of long standing, which they treated, the average number required to make the patient comfortable was 12

Sinus Irrigation

A sinus may be irrigated during the acute stage to relieve pain and occasionally to lower fever, according to Shea. 116 Ventilation should be maintained by local procedures early and irrigation of the sinuses reserved for the cleanup. It is a good practice never to irrigate when the fever is rising but many a protracted cold may be terminated by *lavage of the proper sinus* at the proper time.

Frontal Sinus—The choice of cannula, malleable or fixed, depends on the surgeon. A roentgenogram is necessary as a road map of direction. A small amount of fluid is used and must be displaced by air pressure to avoid pain after the treatment.

Maxillary Sinus — The closure of the natural ostium is one of nature's few blunders, and the improvement of sinusitis demands its dilation Irrigation of an antrum should be done after the fashion which the surgeon can employ with the least amount of pain and with the most thorough result A tray for this purpose may be likened to a golf bag, containing instruments capable of negotiating many angles. He prefers the natural ostium, for by utilizing it one is re-establishing the normal route of drainage.

Sphenoid Sinus—A good rhinologist irrigates the empyemas of the sphenoid sinus the same as those of the other sinuses, following the customary indications and precautions Occasionally he uses a straight needle after locating the ostium with a probe.

External Drainage—In cases of severe involvement in which internal drainage has failed or intracranial or orbital rupture is feared, external drainage of the frontal sinus is necessary. This can be accomplished easily with local anesthesia. The incision for the Lynch radi-

cal operation on the frontal sinus is made and entrance into the sinus accomplished with a small burr. The frontal sinus is emptied of its contents and a small catheter drain inserted through the window thus made.

Van Alyea¹³² recommends *irrigation* of the frontal sinus for acute conditions if after 48 hours the temperature is normal. In subacute conditions with stuffy nose, discharge and cough, he advises a submucous resection and infraction of the middle turbinate preliminary to the irrigation. Six to 8 irrigations are usually required to clear up this type of case Early chronic conditions (3 to 8 months) require the same surgical treatment, but the number of irrigations may have to be extended to as many as 20. Chronic conditions of longer standing wherein tissue changes have taken place require, in addition, an enlarging of the natural ostium. Recurring attacks of frontal sinusitis may be relieved by 1 irrigation but usually need surgical treatment as well. The author has seen no bad results from irrigation and states that many ostiums can be probed for irrigation.

Childrey¹³³ claims very good results in the treatment of maxillary sinusitis of all types by the instillation of *neo-prontosil* following irrigation. He instills 3 to 5 cc of a 2.5 to 5 per cent solution. This he says is absorbed slowly. Consequently it acts on the mucosa of the sinuses for from 36 to 48 hours. For severe attacks with toxic symptoms he gives sulfamilianide orally in addition to the local instillation. He thinks the neoprontosil could be used effectively in the Proetz displacement method in the treatment of the other nasal sinuses.

Diathermy

Short-wave treatment in a number of cases of acute rhinitis, by Brugsch

and Pratt, 134 caused a subsidence of symptoms in all cases but in some there was a recurrence within a few hours. This method of treatment had no effect on allergic types of vasomotor rhinitis. It is valuable, however, in sinus therapy. The nasal blockage is relieved with 1 treatment and the discharge may quickly subside or be considerably reduced. These symptoms may recur after a few months. In a series of 80 cases no change was noticed in the discharge of 26, while in 42 it was lessened or lost its purulent character or ceased. The subjective symptoms, headache, sense of fullness and so on, disappeared under short-wave therapy in all but 11 cases The number of treatments ranged from 7 to 18 and the length of exposure was 15 or 20 minutes.

Referring to short-wave diathermy, the council on physical therapy of the A. M A. states, "In the light of present observations, the consensus seems to be that no physiologic effects other than those attributable to heat have been substantiated"

This according to Hollender¹³⁵ successfully refutes claims made by certain authors that short-wave diathermy possesses peculiar physiologic and biologic properties affecting cellular life. He thinks, however, that the treatment of sinuses by this means produces analgesia through hyperemia and hyperlymphia, improves tissue metabolism, increases resorption and consequently brings about a more rapid defensive response to infection. He undertook an investigation to determine: (a) effect of short-wave diathermy on the temperature in the sinuses (b) The effect of treatment of acute maxillary sinusitis using a controlled group on which other means of therapy were used and a third group using a combination of the 2 types of treatment. He concludes that short-wave diathermy is not a panacea, and only in a few instances has it produced favorable results without the additional use of other measures. The tendency to employ diathermy alone in the treatment of nasal sinusitis is objectionable. Furthermore, its use without an exact diagnosis having been made, as is often the case with certain practitioners, is likely to place this valuable agent in the category of unscientific procedures. When a pathologic process is such that it obviously can be eradicated only by operation, precious time will be lost in seeking to obtain relief from nonsurgical therapy

Roentgen Therapy

Hodges and Snead¹³⁶ stressed (a) the value of the roentgenograms for disclosing unsuspected infections of sinuses and (b) the definite therapeutic value of irradiation for some types of sinus infection. Reviewing the literature on the experimental work done on this subject, they arrived at the following summary of the effect of irradiation on infected membranes of the sinuses "The effect of the x-ray treatment appears to be due primarily to an early destruction of the lymphocytes in the infected membranes From 48 to 72 hours after treatment there appears to be an increase in the number of macrophages

These macrophages are seen to be laden with cellular débris and dead pigments. It is possible they also engulf bacteria. The membrane becomes gradually reduced in thickness but retains numerous plasma cells, polymorphs, and some histocytes. After a week or more some fibrosis appears. There is no evidence of injury to the cilia, epithelium or cellular elements other than the lymphocytes as the result of x-ray dosage.

Hodges and Snead obtained their best results in cases classified clinically as subacute or subchronic, in which symptoms were present for a period varying from several months to several years Many of these patients have a cough and give a history of recurring colds and, on roentgenologic examination of the thorax, exaggeration of the bronchovascular markings of the lower lobes is found. Roentgenologic examination of the sinuses discloses cloudy ethmoids with marked thickening of the membrane in the antra. They obtained good results with irradiation in the majority of cases in which symptoms were present for several years, usually with hyperplastic sinusitis and roentgenographic findings of marked cloudiness of the ethmoids and much thickening of the membranes in the antra. In these 2 groups of cases when roentgenographic exammation disclosed an increase in the bronchovascular markings, small doses of irradiation were applied over the lungs with definite benefit

In the group of cases in which early or reasonably early polypoid changes were found, especially in the nose, with a history of infection for many years, marked relief followed irradiation in the majority of cases. A number had return of the sense of smell and 2 had much improvement in vision following treatment Others who were unable to breathe through the nose were relieved in this respect Some who required repeated operations for removal of polypoid material had no recurrence of polypoid hyperplasia. Usually, the longer the duration of the infection or the more chronic and widespread the polyp formation, the poorer were the results from ırradiation

In the experience of Hodges and Snead, co-operation of the rhinologist and radiologist in the diagnosis, and RHINOLOGY 511

follow-up of the results of treatment were essential for best results.

In the cases characterized by infection, 130 kv. with 6 mm. of aluminum filtration, about 300 r measured in air, was given in 3 or 4 treatments over a period of from 1 to 3 weeks. In those cases characterized by polypoid hyperplasia, 200 kv with 0.5 to 2 mm. of copper filtration, 600 r measured in air, was used.

Sinus Surgery

Before patients undergo radical sinus surgery, they should be made to understand that sinuses are not obliterative in most cases, and because they remain, they are in danger of subsequent reinfection, McQuiston^{1,37} points out. The degree of pathology involving the sinuses and the mucous membrane should always be the determining factors in surgical treatment.

External Operation—So far as the ethmoid cells are concerned, whether the pathologic change is one of suppuration or polypoid formation or a combination of the two, the common practice has been to attack the disease by the nasal route However, Patterson¹³⁸ asserts that operation on the ethmoidal labyrinth through an external incision is becoming a recognized procedure in cases in which the disease is extensive or when one or more operations by the nasal approach have proved unsuccessful The 2 possible objections to the external operation are that it may be more dangerous and that a scar is produced

The author states that by employing the method which he describes, scarring is negligible. In these 'fronto-ethinoidal' cases he relies almost entirely on one or the other of 2 incisions. The "frontal" incision passes along the supra-orbital ridge and corresponds to the center of the hairs evebrow or lies just below it.

The "ethmoid" incision begins about one-fourth inch below the level of the inner canthus at the upper end of a sulcus or natural fold which can generally be seen passing outward and downward into the cheek. The incision is about 1 inch long. The skin should be sliced—not cut vertically to its surface —by holding the blade of the knife parallel to the skin to be incised. In this way a shelving edge of skin is obtained and when the time comes to close the wound such good apposition is obtained that approximation is very accurate and the resulting scar is generally almost invisible. The author states that the results obtained by the external ethmoid operation are most gratifying.

In patients requiring radical treatment an accurate dissection replaces haphazard removal of polyps and bone, which is all that can be accomplished by the nasal route. The patient can be promised a nose permanently free from polyps, and when chronic suppuration is present in the ethmoidal labyrinths, excision of the affected area would appear to be the only certain means of eradicating the disease. The author concludes that none of his patients has developed any serious complications and that meningitis need not be feared provided the operation is carried out with care and precision. A plea for radical operations on the antrum is made by Salinger, 139 who regards the Caldwell-Luc operation "the most uniformly successful and satisfactory operation of the entire small repertoire "

His results in so treating suppurative conditions over a 20-year period have been at least 90 per cent perfect. A great deal depends on the scrupulous care with which the local process is studied and the relation to constitutional factors appraised, the degree of skill applied in its performance and the at-

tention that is paid to disease in the other sinuses.

His procedure in pansinusitis is to follow the Caldwell-Luc operation with transantral exenteration of the ethmoid and sphenoid sinuses, which is easily carried out. The anterior cells, however, must be reached intranasally. The entire nasoantral wall of the middle meatus is removed, a wide passage being thus provided from the operative field into the nasal cavity. If the middle turbinate is hyperplastic or tends to obstruct drainage it is removed in part or completely as the case may be. In such cases, the opening in the inferior meatus is omitted, and the rubber tube introduced into the antrum is pulled through the enlarged middle meatus into the nasal cavity Packing is never employed. If the frontal sinus is diseased it is dealt with through a separate external incision

Salinger thinks that all macroscopically diseased sinus mucosa, including doubtful areas, should be removed. Membrane that looks soft and red, even though it is thin and fairly well attached to the bone, should be taken out, because it is likely subsequently to undergo the same degenerative changes found in the other, more grossly affected, portions. If one has ever seen normal looking mucosa *in situ* he can never forget its pale, almost transparent, glistening appearance.

The Antrum Window—Two things should be considered in the treatment of every patient having maxillary sinusitis, according to Hempstead·140 First, cessation of discharge and, second, restoration of the antral mucous membrane to as nearly normal condition as is possible. Unnecessary destruction of the ciliated epithelium should be avoided A functioning mucous membrane is to be preferred to scar tissue

He is an advocate of the intranasal window operation in the treatment of chronic maxillary sinusitis and states that it is easily and quickly accomplished. with the patient under local anesthesia. The advantages of this operation are: (1) Turbinate tissue is not lost when it is performed. (2) Reaction to it is much less severe than that following the radical operation. (3) It causes a minimal amount of injury to the lining membrane, which is permitted to return to as nearly normal function as is possible (4) Polypoid and badly infected membranes have been seen to return to normal after drainage and ventilation have been established.

The use of the antroscope previous to operating is a great aid in determining the necessity of conservative or radical measures. In Hempstead's report 634 cases of the fenestration operation are gathered from the literature with a good result in 97 per cent.

Osteoma of the Sinuses

Osteoma, although unusual, was noted by Childrey¹⁴¹ in 042 per cent of 3510 roentgenograms of the nasal sinuses The frontal sinus is most often affected by this slow-growing, histologically benigh lesion, which seldom causes symptoms and does not often require surgical intervention The average age of the patients was 46.4 years; men were affected more often than women. Various pathologic conditions were present in these patients, and sinusitis was diagnosed by roentgen examination in 58 per cent of those with osteoma of the sinuses It seems questionable whether sinusitis often is the exciting factor in the formation of an osteoma; but when infection is present it increases the operative risk and may be an indication for surgical removal of the osteoma. When reRHINOLOGY 513

moval is indicated, none of the growth should be left, because of the probability of recurrence. Complete removal may, however, be impossible or, because of dangerous complications, undesirable. The decision whether to proceed transcranially or through the sinus rests with the operator and depends largely on the location and extent of the osteoma. In 4 cases roentgenograms of the osteomas made after intervals of from 9 to 32 months showed no change in them.

Hardy¹⁴² reports 4 cases of cysts of the antrum removed through a Caldwell-Luc opening. It is characteristic of these cysts to have no symptoms referable to the antrum. Two came for treatment of colds and sore throats and 2 were referred for an examination for foci of infection in the upper respiratory tract.

Antra-Alveolar Fistulae

An infection may extend to the antrum through dental necrosis or may follow extraction of a tooth if the floor of the antrum is fractured or overenergetic curetting of the socket is induced.

Ashley¹⁴³ classifies antra-alveolar fistulae as follows: (1) Small uninfected fistulae; they heal readily or 1 suture may suffice to close (2) Small granulating types without infected antra; should be treated by the oral surgeon. (3) Large granulating with antral infection; require close co-operation between oral surgeon and rhinologist. (4) Large fistulae which require plastic operation.

If a perforation occurs at the time of extraction immediate closure is advocated. If a fistula develops leading to an infected antrum, a window is made in the naso-antral wall of the inferior nasal meatus. If in the presence of a large fistulous tract x-rays reveal a thickening of the antral mucosa, a complete

antrum operation is advocated at the time of the plastic closure.

Ashley's technic follows: (a) Caldwell-Luc. (b) Remove fistulous lining and curette away necrotic bone. (c) Smooth alveolar ridge. (d) Cut a flap from palate (Fig. 3) including soft parts and periosteum. (e) Swing flap into place, wedging membrane into the fistulous tract and suture edges. The thick plug of tissue makes a firm closure between the mouth and the antrum and encourages healing by first intention.

Sinus Disease and Eye Disorders

Since there is a paucity of case reports showing an unmistakable connection between sinus operations and the clearing up of ocular disease, Cullom144 presents 6 cases which left no doubt in his mind that sinus disease was the cause of the pathologic condition in the eye. Operation on the sinuses cleared up the visual condition Four cases resembled toxic amblyopias. The patients suffered from marked disturbance of vision The gradual onset and the progressive failure of useful vision indicated ultimate permanent blindness. case there was an inflammatory condition of the vitreous which had been present over a long period. In another there was clear evidence of pressure on the optic nerve from an unresolved empyema of the sphenoid sinus. In this case vision might have been restored by spontaneous rupture The great improvement in the general health of these patients is gratifying While these cases are rare, the author believes that they are more numerous than the few reports indicate. He is of the opinion that every patient with failing vision of obscure origin should receive the benefit of a careful examination of the sinuses, including roentgenograms.

Jatschek¹⁴⁵ cites 4 cases of ocular complications relieved by surgical treatment of a sinus. The complication occurred in 3 cases on the same side as

the affected sinus. There were 3 Caldwell-Luc operations, 1 with ethmoidectony, and 1 ethmoidectomy alone The author states that it was difficult to estab-

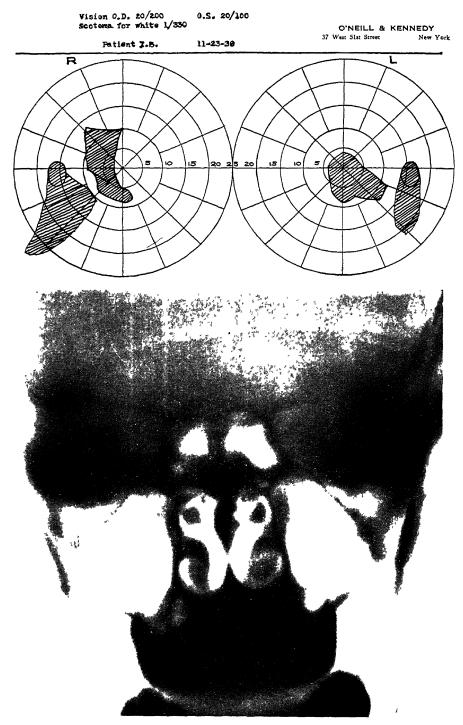


Fig 33—This case at operation revealed a bilateral thickening of the membranes lining the postethmoid and sphenoid sinuses Exenteration of diseased cells was followed by a return to almost normal vision. (Cone, Moore and Dean: Laryngoscope)

lish the relation between the pathologic changes of the eye and those of sinuses. While there may be an anatomic relation between the 2 structures, he is of the opinion that there may have been an infection with a virus that is specific for the uveal tract. He stresses the rôle of focal infection in the case of contralateral involvement.

filmed excluding from the picture shadows from overlying and underlying structures.

Complications of Intranasal Surgery

In a discussion on the complications of intranasal surgery at the Section of Laryngology of the Royal Society of Medicine, Davis¹⁴⁷ said that a good view



Fig 34—In this case all ordinary diagnostic measures failed to reveal sinus pathology Laminagraphs with lipiodol in the antra, however, outlined a polypus and thickened membrane. Following a bilateral radical maxillary and ethmo-sphenoid operation the vision began a steady improvement (Cone, Moore and Dean. Laryngoscope)

Cone, Moore and Dean¹⁴⁶ report the successful treatment of 5 cases of eye disorder by surgical procedures on the nasal sinuses. They were aided materially in their search for diseased areas by use of the laminagraph, a form of body section radiography. By means of this new principle in radiography certain layers or sections of the sinuses may be

of the interior of the nose was essential for good surgery and that anything in the nature of a blind operation was undesirable. He called attention to 4 kinds of injuries that had happened in spite of careful technic. Perforations and injuries to the roof of the nose or to the cribriform plate; injuries to the orbit and its contents, injury to the optic

nerve and injury to the nasolacrimal duct.

Six cases of perforation of the roof of the nose had been recorded and he had seen several in consultation. They occurred with forceps on the ethmoidal cells for sinus suppuration. The perforation in the removal of polypi was always in the region of the posterior ethmoidal cells, when the forceps were directed upward and backward. It was avoided by directing the point parallel to the roof of the nose. The operator might be unaware that the roof of the nose had been perforated, but escape of cerebrospinal fluid or profuse hemorrhage would be a warning. One of the patients in the group suffered from shock and after delayed recovery from the anesthetic complained of intolerable headache and was restless and drowsy. Coma rapidly supervened and death occurred within 3 days, before meningitis had time to develop. The necropsy showed hemorrhage from the posterior ethmoidal artery into the anterior fossa of the skull. The treatment of this type of surgery is the external ethmoidal operation, during which the opening in the dura is covered by a fascial graft. The perforation was inaccessible through the

Hemorrhage into the orbit following perforation of the thin os planum of the ethinoid was the commonest injury. It frequently happened during the ethinoidal operation, particularly on the anterior cells and also in the intranasal frontal sinus operation. The "black eye" was typical and the ecchymosis was maximal at the inner canthus, but if the hemorrhage was considerable, the eyeball might protrude. This might be increased by emphysema. All that was necessary in most cases was to keep the patient at rest in the sitting posture, with the eye covered by a pad and band-

age. The patient should be forbidden to blow his nose for a few days

Injury to the optic nerve in ethmoidal operations produced immediate blindness. Davis had been able to collect reports of 5 cases and had seen 2 of the patients. One injury was caused by evulsion of the middle turbinal and part of the ethmoid in an operation for polypi. Optic atrophy followed, with permanent loss of sight Such cases showed the need for care in the use of the forceps for evulsion. It is safer to use cutting or punch forceps kept in a plane parallel to the outer wall of the nose.

Injury to the nasolacrimal duct had been seen on 2 occasions following an intranasal antral operation The window made in the nasal wall of the antrum extended into the middle meatus above the attachment of the inferior turbinal. severing the duct. On recovering from the operation, the patients complained of blood leaking into the eye. Epiphora and lacrimal obstruction followed. After injection of the lacrimal sac with iodized oil, x-ray examination showed stricture of the duct in the middle meatus of the nose The epiphora was relieved by a dacrocystostomy done above the stricture

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PEDIATRICS

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ANEMIA IN CHILDREN

By Clare R. Rittershofer, A.M., M.D.

Iron Deficiency Anemia

Sedimentation Rate in Nutritional Anemia—Changes in the sedimentation rate of a group of infants and children from 5 months to 6½ years with nutritional anemia due to a deficiency of iron were reported by Carl H Smith 1 The method used was previously described2 and requires the use of capillary blood The value of 36 per cent was regarded as the minimum normal level for the volume of packed cells for the group of children under consideration in terms of which recovery from anemia was to be judged. For hemoglobin the minimum of 10 Gm per 100 cc of blood for the infant has been found to apply to the young child as well The basic red cell count approximated four million red cells. The average rate of settling with the method used was 9 mm, with a variation from 3 to 13 mm mm in 1 hour was regarded as the most rapid rate of sedimentation of normal blood.

The results revealed that the red blood cells in this group of cases did not sediment with the velocity usually ascribed to diluted blood. The most significant observation in the investigation, according to the author, is that anemic blood in nutritional anemia does not behave as does diluted normal blood with regard to the sedimentation rate and that the statement frequently made that anemia is productive of accelerated sedimentation cannot be accepted without reservation. In this type of anemia and

in the age group under consideration, normal rates of sedimentation were observed at times prior to the institution of therapy and usually occurred early in the period of recovery, when the anemia was uncomplicated. When infection supervened, the increased sedimentation rate was further accelerated by the added influence of a lowered cell count. From this the author deduced that when iron in adequate doses is given to a young child with anemia of moderate severity, the persistence of a rapid rate of sedimentation suggests either the continued activity of an infectious process or that the diagnosis of a nutritional anemia is to be questioned. It was also noted that smaller doses of ferrous sulfate than of iron and ammonium citrate were needed to produce a satisfactory response in the hematologic values and a retardation of the sedimentation rate.

Incidence of Anemia - The incidence of iron deficiency anemia of infancy in a large industrial area of Glasgow was investigated by J. H. Hutchison 3 Hemoglobin estimations were made on 300 infants of all ages up to 1 year. The majority of the hemoglobin estimations during the first 2 weeks of life fell into close proximity to the normal curve for that period From the fifth month onwards, however, the individual values with few exceptions fell below the normal, frequently, by as much as 15 to 30 per cent. The principal factors influencing the development of this type of anemia are listed as undue

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prolongation of exclusive milk diet, low birth weight and infections. The author stressed the desirability of the prevention of the anemia not so much on account of the anemia per se but because of the associated high morbidity and mortality rates.

Therapy of Iron Deficiency Anemia-It is now recognized that insufficient iron for hemoglobin formation will lead to anemia of the hypochromic type, characterized by microcytosis and hypochromia of the individual cells, by a low color and volume index, and by a low mean corpuscular hemoglobin concentration. One factor which has tended to produce a more satisfactory and more uniform response to 1ron therapy in recent years has been the more general administration of adequate amounts of iron. The present consensus based on extensive clinical experience favors the use of inorganic iron in large doses

W. M Fowler, and A. P Barer4 reported on balance studies in which the iron intake, the iron excretion, and the hemoglobin regeneration were accurately studied These showed that amounts of iron are retained by the body even when relatively small doses are being administered and that a satisfactory hemoglobin response is obtained in many instances with small doses. M. B. Strauss⁵ has recommended the following amounts of the commonly used iron preparations: Iron and ammonium citrate, 90 grains (6 Gm daily; reduced iron, 45 grams (3 Gm), pills of ferrous carbonate, 60 grains (4 Gm) and ferrous sulfate, 15 grams (1 Gm.) The iron is best given during or immediately after a meal, so as to lessen the gastrointestinal irritation which occasionally accompanies its administration. The effectiveness of the preparation used does not depend on the amount of metallic iron which is being administered, since

soluble forms are better utilized than insoluble preparations with the same iron content. Ferrous salts are more efficient than ferric salts. From the patient's standpoint the smaller effective dose of the ferrous compound is a distinct advantage. Ferrous carbonate is given in pills which should be freshly prepared. The dose is 12 or more 5-grain pills daily. Ferrous sulfate is given in the form of pills with various types of coating to lessen the irritation. Ferrous chloride which has been shown to give a high percentage of retention and utilization may be given in 0.5 Gm. capsules or in solution in a simple syrup. Many other iron preparations are on the market, but none seems to possess a distinct advantage over these common forms These preparations given by mouth are satisfactory without the addition of other metals or other substances.

Moore (loc cit) demonstrated the difference in the availability of various iron salts with the use of iron absorption or serum iron curves following comparable doses of various of the iron salts by When 1ron 1s administered orally, there is an increase in the serum iron which begins within half an hour after administration and reaches its peak at the end of 2 to 4 hours then a slow fall to the normal level. With ferrous chloride and ferrous ammonium sulfate, the serum iron increases compared favorably with those for ferrous sulfate, but very much smaller responses were obtained following comparable doses (3 mg Fe/kilo body weight) of ferric chloride and ferric ammonium sulfate When iron and ammonium citrate was used, the dose had to be increased to 12 mg iron/kilo before the serum iron curve rose enough to fall within the limits defined The reasons given for the lesser efficiency of the ferric salts are: (1) The reduction to the bivalent state

is probably never complete; (2) as soon as ferric iron comes into contact with an alkaline medium, there is formation of the insoluble ferric hydroxide, ferric phosphate, and related salts which automatically removes the iron from availability to the body.

Iron Ascorbate Therapy - D. G. Friend6 carried out a study of iron ascorbate on 21 patients to see whether small intravenous doses were effective. and also whether this preparation could replace the standard compounds in patients who could not tolerate other iron preparations. The iron ascorbate was synthesized according to the method outlined by K. Maurer and B. Schildt.7 The dose employed on the basis of the iron was $\frac{1}{6}$ grain (10 mg.) intravenously and 3 grains (200 mg.) by mouth. This dosage resulted in a daily rise of 1.1 per cent hemoglobin for 15 patients with idiopathic hypochromic anemia. authors concluded that iron ascorbate is an effective form of iron medication, that it can be given intravenously without reaction other than occasional slight flushing and palpitation, and that it brings about a substantial gain in hemoglobin. It also retains some vitamin C properties Intravenously it appears to be as effective in doses of $\frac{1}{6}$ grain (10) mg.) of iron as is ½ grain (32 mg.) of iron as iron and ammonium citrate Orally, 3 to 5 grains (200 to 300 mg) of iron as iron ascorbate is as effective as is 15 grains (1000 mg) of reduced iron or 60 to 90 grains (4 to 6 Gm) of iron as iron and ammonium citrate

Iron-Copper Therapy—J H Hutchison⁸ has given an excellent review of the literature regarding the rôle of copper in the iron deficiency anemias. Metabolism studies were carried out on 9 infants which showed that the administration of copper enhances the conversion into hemoglobin of iron stored

in the tissues and that iron given in doses so small as not materially to raise the hemoglobin content of the blood can be mobilized and converted into hemoglobin by subsequently giving copper. The ferrous sulfate used was given in doses of 1 to 2 drams (4 to 8 Gm.) per week. It was dissolved in water with the addition of glucose to prevent oxida-Copper sulfate (CuSO₄) was given in doses of \(\frac{2}{3} \) grain (40 mg.) per week. The suggestion was made that copper acting as a catalytic agent enables iron to be converted into such a form that it can be transported by the blood plasma from the storage depots to the bone marrow where it can be utilized in the formation of hemoglobin.

Iron-Cobalt Therapy — E. Underwood and C. A. Elvehjem⁹ showed that no increase in growth or hemoglobin regeneration was obtained in rats fed whole cow's milk plus copper, manganese, cobalt, and purified cobalt-free iron in comparison to rats on a similar diet without added cobalt.

Vitamin A in Anemia—F. Mainzer¹⁰ reported on 5 cases of hemolytic anemia and von Jaksch's anemia, of which 2 were treated with vitamin A alone and 3 with vitamin A and blood transfusions Analysis of the blood and bone marrow smears showed that the disease was a disturbance of blood formation rather than a hemolytic anemia. The author believes that vitamin A is an important factor in the pathogenesis of this form of anemia.

Erythroblastosis Fetalis — A case of erythroblastosis fetalis accompanied by hemolysis and edema in a newborn girl has been reported by M T Macklin, J. A Lamont and C C Macklin ¹¹ The authors advance an argument that erythroblastosis is dependent on the rise of a dominant mutation in the germ cells of 1 of the parents. The primary defect

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is the abnormal blood production; the hemolysis is secondary. The mutation for hydrops fetalis causes an abnormal production of blood in the early fetus. This is of such severity that some of the offspring inheriting the mutation die early in the pregnancy, before the opportunity for the formation of edema occurs. Offspring who show hydrops are those in whom the condition is severe but not sufficiently so to prevent development to nearly full term, therefore in such families there would be a large number of pregnancies terminating in miscarriage

The mutation in milder form produces icterus gravis. Here the number of nucleated red blood cells is less and the nutrition is sufficient to allow development to term; but after birth when an excessive number of red cells is no longer needed and the ordinary breakdown occurs, the cells are replaced by large numbers of immature forms. These are hemolyzed since their presence in the circulation is abnormal. The cycle is repeated and, owing to the excessive hemolysis, jaundice and anemia develop.

The mutation in still milder form causes anemia of the newborn. Here the number of nucleated red cells is still smaller, the defect interferes much less with the prenatal development than does either hydrops or icterus and miscarriages in these families are fewer. The fetus comes to term, the destruction of red cells is not so great because the production of new forms is not so exetusive. Jaundice exists in mild degree and the chief symptom is the anemia, since the forms regenerated are for the most part immature rather than mature.

Erythrophagocytosis—The phenomenon of erythrophagocytosis has been reported in 3 infants with anemia of the newborn by T. C. Wyatt, M. B. Cooper and W. A. Groat ¹² Careful search of the smears revealed cells with irregular

outline and light circular cytoplasmic areas which included extraneous matter. In addition to the erythrophagocytes there were also found numerous monocytes with 1 or more possible vacuoles the size of erythrocytes or smaller. The appearance of these cells coincided with the period of severest anemia, leukocytosis, and erythroblastosis.

Hemolytic Anemias - L. G. Parsons¹³ has pointed out that there are examples of acute hemolytic anemia of the Lederer type in infants under 6 months of age which form a connecting link between it and erythroblastosis fetalis. These children were normal at birth, and pallor developed after the disappearance of the normal icterus or later. In addition, these children showed some splenomegaly and an excess of urobilin and urobilinogen in the urine and none ever showed severe jaundice or other signs of icterus gravis; their blood pictures, however, were exactly similar to those of icterus gravis and acute hemolytic anemia. The prognosis in acute hemolytic anemia of the Lederer type is serious, since most of the children die unless treated by repeated blood transfusion, and sometimes even this is meffective

Von Jaksch's Anemia — The author believes that von Jaksch's anemia is not a type of anemia but a blood picture which occurs in erythronoclastic anemia, probably only during the deficiency age period

Parsons gives a review of the hemolytic anemias and expresses a view that these anemias and certain other allied conditions owe their clinical characters to permutations and combination of the erythronic response to an injury; further that fresh combinations may be expected to appear from time to time and that it is incorrect to regard the various forms described by different authors as

hard and fast types and to designate them as separate diseases.

Anemia of Rheumatic Fever—J. P. Hubbard and M. H. McKee¹⁴ noted the blood changes that occur in the anemia of rheumatic fever. Seventeen patients who had a total of 19 recrudescences were studied

An anemia, quite often severe, developed during each of the recrudescences. As the infection subsided, the blood levels tended to rise without any specific therapy and soon reached their former values. The color index remained low. The cell size, mean corpuscular hemoglobin and hemoglobin concentration varied irregularly from low to normal values There is no apparent correlation between the degree of activity of the disease and the amount of serum bilirubin Reticulocytosis of a slight but significant degree occurred after the period of greatest disease activity. This might indicate that a suppression of erythropotesis occurs during the height of disease activity and that when this suppression is withdrawn there follows increased red blood cell formation as indicated by the increase in circulating reticulocytes rapidity with which the anemia sometimes develops suggests that actual destruction of red cells may also be taking place The authors conclude that the presence of anemia may therefore often be an indication of disease activity and should be added to other criteria as leukocytosis and increase in circulatory function in the anemias of children.

It is well recognized that the most important consequence of anemia is reduction in the oxygen-carrying capacity of the blood, but the cardiovascular sys-

tem compensates for the anemia by bringing blood more quickly to the tissues. Although the amount of oxygen carried by each cubic centimeter of blood is small, the total volume supplied to the tissues in each minute is thereby rendered adequate for their needs. The heart and blood vessels are of great importance to the anemic patient and if they fail, the patient may be completely crippled.

Effect of Anemia on Cardiovascular System—Because of the importance of determining how severely the heart is damaged and whether the injury is remediable in whole or in part, C. G Parsons and F. H Wright¹⁵ investigated the cardiovascular function in cases of anemia The study involved the hearts of a group of anemic children during the course of their disease, before and after treatment had been given, watching the effect of therapy on exercise tolerance, vital capacity, venous pressure, electrocardiograms, roentgen measurements of the heart, the oxygen saturation of arterial and venous blood, the circulatory rate, and calculations of the output of the heart.

The results showed that with acute anemia, the tolerance of the child for exercise is decreased, whereas with chronic anemia adaptation to the low hemoglobin concentration may be so complete that practically no impairment of exercise tolerance results. Neither the exercise tolerance test nor measurements of vital capacity are sufficiently accurate or reliable to serve as a measure of the degree of cardiac damage resulting from anemia or to gauge the ability of the heart to recover from such damage through appropriate treatment.

CHICKENPOX

By ROBERT A. LYON, M D

Chickenpox occurring in the first few months of life is rare. An infant 12 days old who had the infection has been observed by E P. Campbell. 16 The mother, who had been exposed to the disease 17 days before the birth of her infant, had developed chickenpox vesicles the day after delivery It seemed possible that the virus had invaded the fetus before birth.

Complications—Encephalitis following chickenpox in a girl, 5 years of age, was reported by R Swyer ¹⁷ Convulsions, delirium, fever, and absent tendon reflexes were noted on the third day after the onset of the rash of chickenpox. The cerebrospinal fluid was under slightly increased pressure and contained 50 lymphocytes and a trace of globulin Recovery was interrupted by an attack of mumps, but proceeded thereafter without any residual symptoms.

Another instance of encephalitis has been reported by H Grenet and P Isaac-Georges. This child, 8 years of age, developed central nervous system complications during convalescence from chickenpox, and the residual symptoms were still present about a year later. Disturbances of equilibrium, an uncertain gait, a positive Romberg sign, a slight

inequality of the pupils and a lateral nystagmus when the eyes were turned far to 1 side, pointed to a lesion in the cerebellum with probably some extension to the medulla and cord. The cerebrospinal fluid was normal. The duration of the symptoms indicated that the damage might be a permanent one, although it was hoped that some improvement would take place in the months to come.

Treatment — An unusually severe case of chickenpox, which yielded to treatment with convalescent serum. has been reported by J Paraf and P. Boulenger 19 A child, 6½ years of age, who developed chickenpox 6 days after the onset of scarlet fever, had vesicles which were unusually round, indurated and were surrounded by large areas of red-The lesions were numerous, painful and accompanied by regional adenitis On the fourth day the condition of the child seemed to be getting worse, so that $\frac{1}{2}$ oz (15 cc) of convalescent serum obtained from a patient who had just recovered from the illness, was injected intramuscularly Improvement occurred rapidly and by the following day, the temperature was normal and a complete recovery was made

DIABETES MELLITUS IN CHILDREN

By Waldo E Nelson, M.D.

Complications—The incidence of hepatic enlargement associated with diabetes mellitus is not high, but its occurrence is much greater during the first 2 decades of life than later. Good results in the reduction of enlargement of the liver with pancreatic extract in 3

children with diabetes mellitus are reported by H G Grayzel and L S Radwin ²⁰ The pancreatic preparation employed was an alcoholic extract prepared according to the method of Dragstedt and co-workers ²¹ Careful control of the diet and adequate insulin therapy had

been unsuccessful in reducing the size of the liver. Blood cholesterol levels were always within normal limits. None of the 3 children had any other complications of diabetes mellitus than hepatomegaly. In each of the 3 children the onset of diabetes occurred in early life, at an age of 3 to 4 years. All 3 had always been short in stature as compared with the averages for their ages. Each child had had 1 or more attacks of acute hepatitis with jaundice which subsided after a time, although hepatomegaly persisted. The attacks of acute hepatitis were not the cause of the hepatic enlargement but were thought to be precipitated by the underlying primary condition of the liver.

The studies of the blood lipids revealed similar findings in all 3 children in that the initial high level of total lipids tended to become much lower after administration of pancreatic extract. A similar tendency was observed in the concentration of the lactic acid and lipid phosphorus of the blood. The values for total free and unbound cholesterol, which throughout the studies were within normal range, remained materially unchanged with or without pancreatic therapy.

Reduction in the size of the liver occurred after from 3 to 5 months of treatment with the alcoholic extract of pancreas. When administration of the extract was discontinued, hepatomegaly recurred. Subsequent administration of the extract resulted again in a recession of the size of the liver to normal. To prevent the development of hepatomegaly in these cases, the authors believed it necessary to administer the pancreatic extract continuously.

A Marble, P White, I K Bogan, R. M. Smith²² have observed gross enlargement of the liver in 60 diabetic children. In this series an enlarged

spleen was also noted in 31 cases. In their opinion, gross enlargement of the liver in diabetic children is associated with and the result of poor control of the diabetes and not with a lack of choline or some other agent derived from raw pancreas. The series was noteworthy for the frequency of complications.

Of the 54 living patients, 38 had had 1 or more attacks of severe acidosis or coma; 42 had had frequent attacks of severe hypoglycemia; 26 were true dwarfs, being 4 inches or more below the standard height for their age: 14 others had infantilism without dwarfism: 9 had arteriosclerosis, as evidenced by sclerosis of the retinal vessels or roentgenologically visible calcification of the arteries of the legs; 1 had cataracts; 7 had had peripheral neuritis; 3 had or had had active tuberculosis; and 15 had had persistent or recurring infections, particularly of the skin or urinary tract Dwarfism, a protuberant abdomen and bouts of abdominal pain were particularly striking features.

The authors are of the opinion that the enlargement of the liver is primary and due to gross fatty infiltration. The condition is considered as unrelated to glycogen storage disease, although the presence of glycogen in amounts approaching the normal is not denied. The possible rôle of hydropic degeneration with retention of water is suggested.

The effect of raw pancreas on the hepatomegaly was observed in 2 children, that of betaine hydrochloride in 12 and that of protamine insulin in 19. No significant change in size of the liver was associated with the use of raw pancreas. With the use of betaine, a variable diminution was seen in 50 per cent of the 12 patients, and with the use of protamine insulin it was seen in 15 or 79 per cent of the 19 patients. Some diminution in size was observed in 1 of 6

patients in the control series. The beneficial effect from the use of protamine insulin was ascribed to the better control of the diabetic condition.

Glucose Tolerance Test — Factors which may modify the response of the blood sugar to the glucose tolerance test are listed by H J. John.²³

Factors Which Tend to Show Improvement in the Glucose Tolerance Curve—

- 1. A restricted diet with reduction of overweight.
- 2. A "free diet" is apt to cause a diabetic curve, a normal glucose tolerance curve will be attained after return to a normal diet
- 3 Absence of fear, when this has been a cause of an abnormal glucose tolerance curve in a previous test
- 4. Disappearance of factors which previously had resulted in delayed emptying time of stomach, thus prolonging the time of absorption
- 5. High glucose tolerance curves may be associated with a state of dehydration
- 6. The latter portion of pregnancy in prediabetics or diabetics
- 7 High carbohydrate, normal Caloric diet
- 8 Thyroidectomy in cases of hyperthyroidism with associated disturbance of carbohydrate metabolism
- 9 General or local increase in the alkalimity of an organism.
 - 10 The administration of alkalis
 - 1 Pyloric obstruction and vomiting

Factors Which Tend to Make the Glucose Tolerance Curve Approach the Diabetic Type—

- 1 Overeating in a patient who has a prediabetic type of glucose tolerance curve.
 - 2. Infections, especially influenza
- 3. A gradual disintegration of the pancreas from any cause.

- 4. Dieting may give a false diabetic curve.
 - 5. Diseases of the liver.
 - 6. Hyperpituitary disease.
 - 7. Hyperthyroidism in some instances.
- 8. Postparturition, in mild diabetics or prediabetics.
 - 9. Carbuncles.
 - 10 Obesity.
- 11. Anything which stimulates the adrenals to overproduction of adrenalin.
 - 12. Osteomyelitis and gangrene.
 - 13. Acidifying diet.
 - 14 Anemia.
 - 15. Arteriosclerosis.
 - 16 Circulatory failure.
 - 17 Emotional upset.

Treatment—Criteria for judging the adequacy of treatment of diabetes mellitus in children are discussed by J. D. Boyd and R. L. Jackson 24 Rigid adherence to diet is required, but the prescribed diet should fulfill all the requirements for growth and activity. The dosage of insulin should be designed to control hyperglycemia at all times. While the instability of the diabetic child does not permit the fullest attainment of this ideal, continuous approximation of normal blood sugar levels has been the authors' criterion in judging the success of management. They have endeavored to avoid glycosuria of any degree as a regular or frequent occurrence and in this regard have been unable to secure adequate control with protamine zinc insulin. They find it necessary to give from 2 to 4 injections daily of standard or unmodified insulin. It is their opinion that if such rigid standards can be maintained, the diabetic child will not be subject to such complications as acidosis, cataract, gangrene or hepatomegaly

Insulin — In answer to criticism of protamine zinc insulin, P. White and L. Winterbottom²⁵ report their experience with the use of this insulin in 123

TABL	EI.
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CONTROL OF DIABETES IN 123 GIRL CAMPERS ON THE SECOND, TENTH AND TWELFTH CAMP DAYS,
MEASURED BY THE RATIO OF DEXTROSE OUTPUT TO CARBOHYDRATE INTAKE

Day of	Number of	Perfect,	Excellent,	Good,	Poor, per cent
Observation	Girls	per cent	per cent	per cent	
Second Tenth Twelfth	123	14	32	25	29
	110	25	49	20	6
	107	32	47	17	4

(White and Winterbottom: J A M A)

diabetic girls in a summer camp. Of these 11 were treated with protamine zinc insulin alone, and 112 with regular insulin plus protamine zinc insulin. Control of diabetes was measured by the amount of dextrose excreted in the 24-hours' specimen of urine and the level of the blood sugar examined fasting, at 11 o'clock in the morning and at 4 in the afternoon. All 3 analyses were usually made on the same day.

Control of diabetes based on the amount of dextrose excreted in 24 hours was classified as perfect, if the patient was aglycosuric, excellent, if the output in grams of sugar was 10 per cent or less, good, if from 10 to 20 per cent; and poor, if more than 20 per cent. The results are tabulated in Table 1 The average blood sugar levels were reported as being nearly normal for the specimens taken at fasting, 11 o'clock and at 4 o'clock There were fluctuations in the amount of glycosuria Thus, 5 of the 13 groups divided according to age showed more sugar in the urine on the twelfth than on the tenth day, although the diet and insulin were essentially unchanged Severe hypoglycemic reactions occurred in 15 per cent, but 85 per cent showed none or only very mild ones. The carbohydrate of the diet in the 2-week intervals exceeded 200 grams in 80 per cent of the cases. Controlled exercise and the lack of opportunity for dietary indiscretions were thought to be important aids in the diabetic control. A few children required supplementary doses of regular insulin at noon or in the late afternoon.

A new insulin compound with a prolonged action on blood sugar has been subjected to clinical trial by H. M. Feinblatt ²⁶ Hexamethylene tetramine was added to standard insulin in the proportion of 0.25 grain of hexamine to 1000 units of insulin. It is claimed that a single daily dose of hexamine insulin produces a blood sugar curve in diabetic patients similar to the one produced by 4 divided doses of standard insulin, but with decided constriction in the range of the fluctuations of the blood With protamine insulin the average blood sugar level at 6.00 A. M. was 120 mg. per cent as compared with an average level of 180 mg. per cent with hexamine. However, the higher blood sugar levels, which occurred for the first 8 hours after injection of protamine insulin, did not occur after injection of hexamine insulin In general with single daily injections of hexamine insulin, the average daily blood sugar curves fluctuated between 140 and 170 mg. per cent throughout the entire day.

DIGESTIVE SYSTEM

By Waldo E. Nelson

Stomatitis

A clinical study of acute infectious stomatitis in children has been carried out by W. C. Black 27 The term "acute infectious gingivostomatitis" is proposed for infection of the mouth in children which is characterized by marked gingivitis, oral fetor, fever, and enlargement of the regional lymph nodes In the author's series, the etiologic factors could not be determined. It appeared unlikely that the oral anaerobic organisms, including Vincent's fusiform bacillus and spirillum, played more than a subordinate rôle in the pathogenesis Oral anaerobic organisms of various sorts were found to be constant inhabitants of the anaerobic crevices of the normal mouth, even in young children While they may temporarily increase in number during any gingival inflammation, individually and collectively they appear to be essentially harmless for laboratory animals

It was found that an acute infectious gingivostomatitis affected the hardy and well-kept child as commonly as it did the malnourished and dirty. It occurred most commonly in the fall and winter months and the incidence was about twice as high in girls as in boxs. The peak of incidence was at 30 months of age, while in four-fifths of all the cases the disease occurred before the fourth birthday Fever, the symptom most commonly present at onset, often preceded the appearance of local lesions by 1 to 3 days The gingivitis and oral fetor frequently reached their peak of intensity after the constitutional symptoms had subsided. More than half of the patients had little, round, shallow oral, or labial ulcers The disease is benign and selflimited. Recurrence and second attacks

are rare. No important complications were encountered in the author's series.

There is no specific treatment for acute infectious gingivostomatitis. The general symptomatic treatment consists of rest in bed until the temperature is normal; adequate fluid intake; administration of sedatives and acetyl salicylic acid when necessary; and a soft or liquid diet, which is not salty, spiced, acid, or The author states that if there is any important feature of the care of the mouth, it is cleanliness. However, in young children, during the height of the disease, it is often impossible to apply successfully any local treatment. As improvement sets in, a very soft toothbrush with a mild, nonirritating soapy dentifrice may be employed gently Caustics should not be applied to the inflamed gums, since they may cause destruction of tissue with subsequent retraction of the gums Oxidizing agents, such as dilute hydrogen peroxide and sodium perborate, discourage the growth and multiplication of oral anaerobes and serve the further purpose of diminishing the disagreeable odor. No benefit is derived from the local application of arsphenamines, either dry or in solution

Tannic acid jelly is recommended by I Mirvish²⁸ in the treatment of infectious stomatitis in infants. The type of lesions for which this treatment is advocated may vary in severity from a few small aphthae on the tongue, cheek, or lip, associated with a little irritability and anorexia, to the more severe cases characterized by intense inflammation of the gums, oral fetor, fever, and acute swelling of the regional lymphatic nodes. A proprietary tannic acid jelly, such as used for burns, is employed by the

author. The mother is instructed to scrub her hands thoroughly with soap and water and then to apply a little of the jelly to the child's gums and teeth with her fingers. Applications at from 2- to 3-hour intervals are recommended, but more frequent applications are quite safe.

Thrush—J. H. Ebbs²⁹ emphasizes that thrush is not always a benign infection In 28 cases of esophagitis in infants observed by him, 22 were caused by thrush The outstanding clinical features were the presence of oral thrush, refusal to take feeding, vomiting during or soon after feeding, severe toxemia, pallor, and weak pulse and, in some instances, the presence of blood in the vomitus, and occasionally melena The pathologic process was one of ulceration of the epithehum and invasion of the submucosa by the mycelium of the thrush fungus He advises local treatment of oral thrush with gentian violet (1 per cent aqueous solution) and if an esophagitis is suspected, a more than usual generous application to the lesions of the mouth with the hope that some of the solution may reach the esophagus.

Vomiting

From a metabolic and clinical study of children subject to recurrent attacks of vomiting, J. A. Johnston and R. J. Mason³⁰ were unable to find any single defect which would explain the cause of Mention is made of such the vomiting possible etiologic factors as focal infection, emotion, postural defects, visual errors, and gastroenteric abnormalities which should be thoroughly appraised From their studies they concluded that these children as a group were prone to have depleted reserves of glycogen between attacks. They advise such prophylactic measures as regulation of activity, removal of foci of infection, and proper diet. During attacks, they recommend

the use of *insulin* in addition to the conventional *glucose* and *saline* treatment. It is emphasized, however, that insulin must not be administered in such a situation, unless adequate amounts of normal saline have preceded the administration of glucose.

Diarrhea

Bacterenia due to Bacillus dysenteriae occurring in 3 infants is reported by K. Dodd and H. Swanson.³¹ Comparatively few such cases have been reported; in fact, the usual statement found in textbooks on bacteriology and pathology is that bacterenia due to this organism does not occur. The authors point out that the finding of dysentery organisms in the blood stream may prove to be an aid in the differential diagnosis between bacillary dysentery and some forms of typhoid fever.

In an article on the therapy of diarrhea in children, A G Mitchell³² has outlined a plan of therapy to be employed in the ordinary cases of gastroenteritis:

Mild Gastroenteritis Without Vomiting in an Infant Aged 6 Months—The first day, nothing by mouth for 24 hours except water, 5 per cent dextrose solution or physiologic salt solution, which should be offered in amounts of 3 ounces (90 cc) every 3 hours, but without forcing Hypodermoclysis of 6% ounces (200 cc) or more of physiologic solution of sodium chloride or 5 per cent dextrose solution is given twice a day

The second day, if there is some improvement, half strength skim milk, skimmed lactic acid milk, or protein milk, about 3 ounces (90 cc.) every 3 hours, with 5 per cent dextrose is offered between feedings. Hypodermoclysis is given if necessary

The third day, if improvement continues, full strength skimmed milk is given.

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After several days, the formula is slowly increased to full strength. Sugar may be added to the formula on the fourth or fifth day, orange juice, and cod-liver oil being added at approximately the same time.

Severe Gastroenteritis and Marked Dehydration with Some Vomiting in an Infant Aged 6 Months—In addition to the treatment outlined for a mild case, the following procedures are suggested:

Five per cent dextrose in physiologic solution of sodium chloride is given intravenously. Other balanced salt solutions may be used.

Transfusions given after the anhydremia has been partially corrected. The total fluids in the 24 hours to be approximately 3 ounces (90 cc.) per pound of body weight.

Fluids by mouth limited to from ½ ounce (15 cc) to 1 ounce (30 cc) of 5 per cent dextrose every 3 hours

Determination of the carbon dioxide content of the blood and correction of acid-base balance if necessary *Calcium gluconate* from 5 to 10 cc of 10 per cent solution intravenously if there are convulsions

Continued good results with *pectinagar diet* in the treatment of diarrhea of infants and children are reported by M. Winters, C. A. Tompkins and G. W. Crook ³³. The preparation consists of

Pectin 6 3 per cent Agar agar 4 3 per cent Dextrimaltose 89 4 per cent

These are mixed together in the dry form, which is used in the milk for the feedings of infants or older children. Two basic forms of feedings are employed. A fluid form, which is used for the nursling or for lavage purposes, is made in the proportion of 1 cup of the pectin-agar powder to 24 ounces of milk. For the older child who is spoon fed, a more concentrated combination of 1 cup of the

powder to 16 ounces of milk is employed. The milk is added slowly to the powder and the combination cooked in a double boiler 10 to 15 minutes with occasional stirring. The more fluid form is placed in nursing bottles in the quantity desired for each feeding. When cold, this forms a soft gel, which upon reheating and shaking, will break down into a smooth, thick liquid and can be fed through a nipple with an enlarged opening. When necessary, such flavoring as chocolate, vanilla, or peppermint, or sliced bananas or banana powder or various colorings may be added to overcome the objection of older children The authors have had equal success when skimmed milk, onehalf skimmed milk, or even whole milk, was employed as the diluent.

The pectin-agar feedings were given to the infants at the time of admission to the hospital, there being no starvation period. No other food was given by mouth except glucose water which was not restricted. When indicated, parenteral fluids were administered.

The authors report a definite and quick response to this type of therapy with soft stools within an average of 34 hours. In their series there was a gradual and steady improvement in 73.4 per cent of the cases. The Caloric intake averaged from 33 to 52.4 Calories per pound per day, and average expected weight gains were frequently observed.

Details for the use of apple powder in infant feeding and in the treatment of diarrheal diseases has been outlined by I. A. Manville 34. When cow's milk is used for the formula, evaporated milk is diluted to twice its volume with water containing 10 per cent apple powder. The water is prepared by placing 2 moderately heaped teaspoonfuls of apple powder in an 8-ounce container. Water is added slowly, and the mixture is constantly stirred. The formula thus con-

tains 5 per cent apple powder. This is the maximum amount which can be added without interfering with the passage of the formula through the openings in the rubber nipple.

For older children and adults, all food is withheld for 3 to 4 days, during which an 8-ounce glass of water containing 10 per cent apple powder is administered at 3- to 4-hour intervals At the end of this period the transitional diet is started. Custards that have been prepared with milk containing 5 per cent apple powder and gelatin desserts made with water containing 15 to 20 per cent apple powder are fed. These foods, together with applesauce or baked apples, occupy a rather prominent place in the menu for 2 or 3 days after the discontinuation of the apple powder water. Buttermilk and cottage cheese may be added gradually. Protein foods are restored to the diet last and with caution.

Allergy

B Ratner and H L Gruehl³⁵ have shown that certain grain products when subjected to moist heat undergo a change which results in allergenic denaturation The effect of heat on the antigenicity of foods depends, first, on the heat stability or heat lability of the different molecular components and, second, on the length of time they are heated and the type and degree of heat used. On the basis of their animal experiments, the authors believe it possible that certain heat-treated grain foods may be used in selected cases of They suggest that diets free from wheat and from other grains should be revised to include the allergenic denatured foods The incorporation of these foodstuffs in the diets of persons sensitive to foods may aid in establishing better nutrition and avert the introduction of psychologic feeding problems.

By means of serial titrations, the fluctuations of passive transfer antibody titer have been studied in children hypersensitive to food by V. W. Lippard and W. M. Schmidt.³⁶ Ingestion of foods to which patients were hypersensitive was followed by increase in titer of passive transfer antibody, when antigen sufficient to produce clinical reactions was absorbed. The absorption of specific antigen appeared therefore to be capable of augmenting the production or mobilization of this antibody in the blood serum. Clinical reactions to absorption of specific foods were less frequently observed and less pronounced after an increase in titer of passive transfer antibody. This evidence suggests that in human beings protection of sensitized tissues from manifestations of hypersensitiveness may be associated with a rise in titer of circulating passive transfer antibodies.

Celiac Disease

A study of the clinical manifestations of 35 infants in whom an advanced lesion of the pancreas was found at necropsy has been made by K D Blackfan and C. D May. 37 The pathologic changes consisted of inspissation of secretion, dilatation of the ducts and acini, atrophy and fibrosis The infants in this series of cases, with the exception of 5 who died soon after birth, either failed to gain or lost in weight. There were frequent attacks of diarrhea but death appeared to be due to a widespread pulmonary infection. In 7 of the infants there were symptoms commonly associated with the celiac syndrome, such as wasting, especially apparent in the buttocks and thighs, distention of the abdomen, and fatty stools. The average age at death of these 7 infants was 20 months in contrast to the average of 8 months of age for the remainder of the group. In a discussion of the relation of vitamin A to

TABLE II

CLASSIFICATION OF COOKED CEREAL FOODS AND BREADSTUFFS ACCORDING TO THEIR

ANAPHYLACTOGENICITY.*

Allergenic V	Vheat	Allergenically Denatured Wheat			
White bread Rye bread Ordinary toast Zwieback Crackers (all varieties) (all varieties) Pretzels Matzoths Waffles Pancakes Cakes (all forms) Piecrust Pastries		Multiple precooked dry cereal Various precooked wheat cereals Wheat and multiple ce- reals cooked in a double boiler †	Spaghetti, macaroni, noodles† Melba toast Rye biscuit Dextrimaltose Wheat and multiple cereals cooked in a double boiler†		
Rye		R	ye		
Sour rye bread Ordinary rye bread Pumpernickel	Swedish rye bread Rye biscuit Pancakes				
Corn		Corn			
Cooked corn meal Canned corn Corn on cob Corn starch pudding Corn fritters Pancakes Corn breads		Precooked corn cereals	Popcorn Corn syrup		
Rice		Rice			
Boiled rice Rice pudding Precooked rice cereal A	e pudding Rice fritters		Cooked brown rice		
Barley		Barley			
Malt extracts and brews Malted cereals Malted milk preparations	Pearled barley Barley water	Dextrimalto-e			
. 11					

^{*} We were unable to sensitize animals with out Out products, therefore, are not included in this chart. The unstandardized methods of preparation of home-cooked products militates against their use by the exquisitely sensitive person.

(Ratner and Gruehl Am J Dis Child)

this condition, the authors point out that while the efficiency of absorption of vitamin A appears to be diminished and in such cases an excess amount should be given, it should not be construed as indicating that a vitamin A deficiency plays an important part in the production of the pancreatic lesions described.

While too little is known of cystic fibrosis of the pancreas to establish a definite plan of treatment, D H Andersen³⁸ indicates several factors which should be taken into account in planning the treatment of a given case (1) The children in her series who survived the first few months of life were those who

received mothers' milk with the addition of cod-liver oil or other vitamin A and D preparations and who were later given a diet for celiac disease. (2) The frequency of vitamin A deficiency is taken as an indication that large doses of fatsoluble vitamins should be administered. In some instances, it may be advisable to give them parenterally. While a diet low in fat appears to produce improvement in the stools, the hazard of vitamin A deficiency and pulmonary infection is so great that it seems unsafe to employ it. Fatty stools are preferable to fatal purulent bronchitis. (3) Experiments on ligations of the pancreatic duct in dogs have demonstrated that the animals require a greater quantity of food than normal to maintain health The absolute amount of food which is absorbed increases with the amount ingested, although the proportion decreases. Andersen suggests that this observation be applied in these cases of pancreatic insufficiency and that the Caloric intake be in excess of the usual amount for the age

Treatment, according to S V. Haas, 39 is exceedingly simple and consists of diet alone A few principles must be borne in mind No milk as such may be permitted and no sugar or starch in any form excepting as it occurs in bananas and oranges and in protein milk and calcium caseinate milk or cottage cheese. I'rotein may be used in any form, such as meat, egg white, gelatin, protein milk, calcium caseinate milk, and cottage cheese His basic diet is as follows Breakfast orange juice, cottage cheese, bananas, protein milk for children less than 2 years of age, and calcium casemate milk for older children and adults, in any quantities desired by the patient Lunch -meat, liberal portion, preferably broiled or roasted Bananas, protein, or calcium casemate milk, and sugar-free gelatin. Supper—the same as breakfast, or egg white and bacon may replace the cheese. Saccharine should be used for sweetening. Between meals—the milk preparations and bananas may be given. At a later date, vegetables, except potatoes and other fruits, may be tried very carefully, one at a time. As a rule vegetables are not very well tolerated early in the treatment.

This diet, even in the face of apparent normality, should be continued for at least a year, when starch in the form of toast or cereal may be tried. If any symptoms, such as diarrhea, anorexia, or irritability, appear, these foods should be discontinued at once. If no ill results have followed by the end of 3 months, plain milk may be added with the same precautions.

If there have been no ill results at the end of another 3 months, then a full diet may be used and it should be well tolerated. Sugar should be restricted in quantity for a long time.

There is said to be a variation in the tolerance for fats. Butter, as a rule, can be used early and freely; sour cream is better tolerated than fresh cream; but cod-liver oil is not tolerated at all

The only vitamin recommended is vitamin D in concentrated, preferably dry form No statement is made concerning the adequacy of vitamins A, B, and C in the diet prescribed.

Megacolon

A clinical study of considerable interest on the treatment of megacolon, with associated constipation, by means of drugs acting on the sympathetic and parasympathetic nervous system has been carried out by W () Klingman.⁴⁰ Neither surgical nor medical treatment has shed any light on the etiology of megacolon other than to demonstrate that it probably arises from an unbalance of the autonomic nervous system. Kling-

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man suggests that, clinically, idiopathic or acquired megacolon falls into 1 of 2 groups, excluding mechanical obstruction of the colon First, there is a group termed rectosigmoidal achalasia, in which there is a failure of the rectosigmoidal apparatus to relax. In the other group there is a failure of the motor function of the parasympathetic system to act effectively above the rectosigmoidal region The separation of cases into these 2 groups and their respective subdivisions is made on the basis of roentgenologic examination with barium enemas and by trials of appropriate drug therapy. The author's classification is as follows:

- (1) Cases of rectosigmoidal achalasia (a) Those caused by motor hyperactivity of the sympathetic innervation to the rectosigmoidal apparatus (cases which are not influenced by any known or tried medications), (b) those caused by ineffective inhibitory function of the parasympathetic innervation to the rectosigmoidal apparatus (cases which respond to parasympathetic paralysants, as, for example, syntropan)
- (2) Cases of deficient motor function of the innervation of the colon above the rectosigmoidal apparatus (a). Those caused by deficient parasympathetic motor function (cases which respond to parasympathetic stimulants as, for example, prostigmine), (b) those caused by deficient sympathetic motor function

Clinically, the 2 types of rectosigmordal achalasia cannot be distinguished except after trial of appropriate drug therapy. However, by barium enema studies, it is frequently possible to demonstrate whether or not there is rectosigmordal spasm with or without delayed emptying of the colon. In cases of rectosigmordal achalasia there is marked delay in emptying; whereas in the cases where there is deficient motor function on the part of the parasympathetic supply of the colon above the rectosigmoidal apparatus, there is good emptying of the lower colon but retention of the barium in the upper colon.

Based upon the above classification, the author proposes a selective form of treatment for each of the conditions classified. When x-ray interpretation has established the fact that the rectosigmoidal apparatus is functioning, prostigmine should be tried. If the rectosigmoidal apparatus is not functioning, bezedrine sulfate should be tried first and then syntropan. If there is no response to either of the latter drugs, it is proposed that resort be made to surgical treatment by lumbar ganglionectomy and presacral resection.

G. de Takats and A. D Biggs⁴¹ feel that with the introduction of sympathectomy in the treatment of megacolon, many of the objections against surgery will have to be revised. They state that if intensive, conservative therapy is instituted, including daily irrigations, rectal dilatations and parasympathetic drugs, many children with this condition respond well However, for the intractable cases, after the age of 3 years, sympathectomy should be considered They also caution that this procedure has its limitations and may have to be followed by removal of parts of the colon, usually the sigmoid loop

Intestinal Obstruction

In an extensive article, R McIntosh and E J Donovan⁴² discuss the clinical aspects of disturbances of rotation of the intestinal tract. They report 19 cases with the syndrome of organic ileus. In most instances there was a clear-cut picture of duodenal obstruction and in 1 case gross intestinal hemorrhage. All were traceable to errors of intrauterine development of the midgut. They point out that the cause of intestinal

obstruction may lie in volvulus of the entire portion of intestine which arises from the midgut loop or of a large section of it, in the persistence of peritoneal bands which distort and constrict the duodenal channel or in combinations of these. Symptoms are apt to occur within the first few days of life. In certain instances, however, there may be a delay in their appearance, and in some, the symptoms may be ameliorated and disappear spontaneously only to return at

a later date. The authors believe that spontaneous improvement in these cases often denotes that a loose twist of the intestine has resolved itself. It is suggested that such episodes may be frequently repeated and may give rise to a serious diagnostic problem. They emphasize the fact that all cases of duodenal obstruction as well as those of "periodic vomiting" should be investigated by appropriate study, especially by proper use of roentgenographic technic.

DIPHTHERIA

By ROBERT A. LYON, M.D.

Mortality—Diphtheria mortality rates throughout the United States have continued to decline. The annual report⁴³ of deaths in large cities has indicated that 1938 was the twelfth consecutive year in which a decline in the death rate has taken place. The rate for the year 1938 in 93 cities was 1.23 per 100,000 population as compared with 1.46 in 1937 and the actual number of deaths decreased from 568 in 1937 to 483 in 1938 The best record was made again by the cities of the Middle Atlantic States (0.48 deaths per 100,000 population) Twenty-four cities had no diphtheria deaths during the year 1938

Clinical Types — Diphtheritic infections of the skin and conjunctiva have been observed in a series of 11 patients by H. R. Rogers ⁴⁴. These infections frequently occurred in association with streptococcus infections and were noted occasionally in patients with scarlet fever, erysipelas and measles. From his observations, the author concluded that chronic lesions such as impetigo which does not heal readily or conjunctivitis of unusual tenacity should lead to a suspicion of a diphtheritic infection. The treatment of his patients with antitoxin usually resulted in a rapid improvement of the local conditions.

A diphtheritic infection of the lip occurred in a patient of H. J. Lavender and J B Squires.⁴⁵

Diphtheritic pleuritis, a rare form of the disease, has been observed recently by W. J. Davies. 46 Six reports of such diphtheritic infections in patients ranging from 3 to 51 years of age were found in the medical literature and only 2 of these patients had survived. It seemed probable that the diphtheria bacillus invaded to cause a secondary infection in most instances.

Complications — Various types of postdiphtheritic paralysis which occurred in 9 children were reported by J. M. Arena and L. P. Rasmussen ⁴⁷ Of especial interest was the fact that 6 patients had such mild attacks of the disease that it had not been recognized. In 7 instances the diphtheria bacilli were still present in the nose and throat cultures. In the different patients, the paralysis had involved the palate, larynx, face, diaphragm and extremities. Two deaths occurred, apparently due to myocardial

failure. Treatment with antitoxin and glucose solutions seemed to have definite effects in hastening convalescence, and symptomatic treatment included adequate rest with the aid of sedatives, gavage of patients with palatal paralysis, and use of the Drinker respirator for those with respiratory embarrassment.

Diagnosis — Employing 7 different morphologic and cultural tests to differentiate the various types of diphtheria bacılli, M. Frobisher, Jr.48 found that of the 237 strains isolated from residents of the city of Baltimore, 4 could be classified in the gravis group, 100 in the mitis group, and 133 into the intermediate types. While the gravis strains had all 7 of the characteristics of that group, the intermediate strains had anywhere from 2 to 6 characteristics of gravis forms. The conclusion was reached that the classification of the various diphtheria organisms should be enlarged to express the gradations from very mild to the severe forms of bacilli If the classification of diphtheria bacilli were based upon more standard and accurate criteria, the data from various parts of the world could be compared more readily The large proportion of mitis and intermediate types of the diphtheria baall which occurred in the author's group of patients may have been the result of a lowered morbidity rate of diphtheria and possibly an evolutionary change of the bacillus due to changes of the host-parasite relationship, but it was impossible to make any comparisons with past experience since this type of classification had not been conducted prior to the year 1933

The strains of diphtheria bacilli isolated from 325 patients in Australia by H Wilson and N E Goldsworthy⁴⁹ indicated that the gravis types of the bacilli occurred more frequently in severe

types of the disease. Mortality rates were higher in the 109 patients who had this type of infection than in the other groups. In 18 patients with malignant diphtheria the majority had infections with the gravis strain of bacillus and 12 patients of the group died

Differences in the morbid anatomy of 51 patients infected with gravis, mitis or intermedius types of diphtheria bacilli have been recorded by J. W. McLeod. J. W. Orr and H. E. deC. Woodcock.50 The most striking differences between the 3 types of infections were noted in the local lesions, where gravis and intermedius bacillı caused much deeper penetration, more disintegration, more extensive inflammation, and greater involvement of cervical lymph nodes than the mitis varieties. Laryngeal obstruction was caused more frequently by the mitis organisms but invasion of the lungs and toxic changes of the heart and kidneys were more commonly associated with the gravis and intermedius types of bacıllı.

An immediate test has been proposed for the differentiation of a diphtheritic membrane from other exudates. It has been claimed that a 2 per cent solution of potassium tellurite applied to an exudate will cause a blackish discoloration within 10 to 30 minutes if the diphtheria bacillus is the etiologic agent and no discoloration occurs if other bacteria are the cause Clinical tests with this diagnostic procedure have been made by E. Tomlin⁵¹ in a series of 46 patients and by J. B. L. Tombleson and R. M. Campbell⁵² in a group of 200 patients. In the majority of patients, the black discoloration occurred only in the case of diphtheritic infections Occasionally, however, exudates caused by other microorganisms turned black and a few diphtheritic membranes failed to give the characteristic color change It is necessary for the tellurite solution to be fresh in order to be effective. The authors did not believe that the test would ever replace the customary clinical and bacteriologic methods of diagnosis but in some instances, it might give some assistance in making a rapid decision in regard to the etiologic agent.

Treatment - Concentrated antitoxin consisting of the globulin fraction of horse serum has been employed universally in recent years for the treatment of diphtheria. A question of the comparative value of this serum with the older nonpurified types of serum has been raised by B. A. Peters.⁵³ For the past 6 years he has treated alternate patients with the nonpurified natural serum and compared the results with those obtained with the concentrated globulin types. The sera were administered intravenously together with a 20 per cent glucose solution. In the series of 135 patients receiving the natural serum and the 148 receiving the concentrated forms, the mortality rates and the incidence of paralysis were approximately the same Severe reactions to the serum occurred in 23 per cent of those receiving concentrated serum and in only 11 per cent of those receiving the larger quantity of protein in the unconcentrated serum Late serum rashes were also slightly more common in the group receiving concentrated types. It was suggested that the concentration of the serum had destroyed some of its natural colloidal properties and made it more toxic for intravenous use Other types of sera, however, such as streptococcal antitoxin, had not appeared to be affected by concentration in the same manner.

Highly refined diphtheria antitoxin was effective in combating the illness and caused very few reactions in the 200 patients observed by A. Hutchison.⁵⁴ The antitoxin had been purified by enzymatic disintegration and differential heating. It was given, without preliminary testing of the patient for sensitivity, to 100 children by the intramuscular route and to the other 100 by intravenous or combined routes. No serum reactions occurred and only 1.5 per cent of the group developed fever responses. Mortality rates in this series of diphtheria patients and the incidence rates of paralysis were lower than many previously reported epidemics of the disease.

Prevention—The administration of toxoid together with antitoxin in the treatment of patients with diphtheria has been advocated by G Ramon⁵⁵ to stimulate the production of an active 1mmunity. It was hoped that such an immunity would aiminish the frequency and severity of late manifestations of the disease The early administration of antitoxin is highly essential for the immediate treatment of the disease but the serum is eliminated so rapidly that subsequent injections are required which often cause unfavorable reactions The inclusion of toxoid in the first injection should lead to the slow development of an active immunity which might prevent recurrences and relapses of the disease and possibly prevent complications.

From previous observations, the procedure of combined treatment has been effective and without danger of severe complications. The presence of the toxoid has not inhibited the action of the antitoxin nor has the presence of the antitoxin prevented the development of active immunity produced by the toxoid. The toxoid was administered first in a dosage of 0.1 cc subcutaneously and within 20 to 60 minutes the antitoxin was given at some point distant from the first injection. About 48 hours later,

if the patient's reaction has not been severe, a second toxoid injection of 0.5 to 1.0 cc. was given and at 5-day intervals doses of 1.0, 2.0 and 3.0 cc. of toxoid were administered, the size of the dose depending upon the previous reaction of the patient.

Studies of this form of therapy have been made by R. Martin, A. Delaunay and R. Richou⁵⁶ in a series of 12 children; and H. Darre and A. Laffaille⁵⁷ in a series of 33 patients with the disease. They noted a freedom from severe reactions, no evidence of interference with the normal action of the antitoxin; a reduction in the number of complications of diphtheria, and the development of high titers of antitoxin in the blood.

A comparison of fluid toxoid and alum precipitated toxoid as immunizing agents has been made by V. K Volk and W E Bunney 55 Measurements of the immune response of the children were made by blood antitoxin determinations. Two injections of alum precipitated toxoid administered at intervals of 3 weeks produced adequately high titers of antitoxin in 100 per cent of a group of 148 children. Three injections of fluid toxoid at 3-week intervals caused an increase in circulating antitoxin in 98 per cent of a group of 162 children within 4 months after inoculation and 96 per cent of this series still had increased titers of antitoxin at the end of 12 months. Less satisfactory results were obtained with single or double injections of fluid toxoid or with single injections of alum precipitated toxoid Although fairly large percentages of children responded with antitoxin increases with this latter number of moculations, they failed to maintain the levels for more than a few months.

A study of the efficacy of various immunising agents for diphtheria has been

conducted by H. N. Bundesen, W. I Fishbein and J. L. White ⁵⁹ In 5 groups of children who had received different antigens for protection against diphtheria, Schick tests and blood antitoxin determinations were made. All but 2 of a group of 125 children who had received 3 toxin-antitoxin injections about 6 years previously had negative Schick reactions, and 74 per cent had more than $\frac{1}{25}$ units of blood antitoxin. Among 125 children who had had 2 injections of toxoid about 4 years previously, positive Schick reactions were noted in 19 and about 63 per cent had ½5 units of blood antitoxin. In the third group, which had received 2 doses of alum toxoid 1 week apart, 2 to 3 years before, positive Schick tests were more numerous and about 63 per cent had ½5 units of blood antitoxin. Those who had had only 1 dose of alum toxoid 2 years previously had the smallest incidence of individuals (43 per cent) with $\frac{1}{25}$ or more antitoxin in the blood The children who had received 3 injections of plain toxoid at monthly intervals had had the highest percentage of individuals with $\frac{1}{2}$ units or more of blood antitoxin.

The conclusions drawn by the authors were that several injections of an antigen at widely spaced intervals gave the best immune response on the part of the patients. They had had the most success with plain toxoid. It seemed practical to raise and to maintain higher levels of antitoxin in the blood than were measured by ordinary. Schick reactions

The relative values of unmodified and alum precipitated toxoids as immunizing agents in guinea pigs have been compared by F. G. Jones ⁶⁰ It was his conclusion that any such material should contain at least 15 Lf units per dose. The alum precipitated toxoid was the most effective material and 1 dose of

it was better than 2 of the unmodified toxoid although not so effective as 3 doses of the latter material.

Long intervals between injections were recommended. In the case of unmodified toxoid, 2 months seemed an adequate interval but after alum precipitated toxoid was given, an interval of at least 3 months was recommended before either another alum precipitated or plain toxoid injection was administered.

Single doses of alum precipitated toxoid may be adequate for 1mmunization of children living in areas where diphtheria is not endemic. A. S. Dean and S. Hyman⁶¹ gave a single injection of this antigen to 302 susceptible children who had never received the immunizing injections previously 89 per cent were Schick negative 28 months later. A group of 140 children previously treated but Schick positive was given a single dose of alum precipitated toxoid and 98 per cent were negative 28 months later. About 95 per cent of a third group, whose immunity status was not determined, were Schick negative 28 months after the single dose of alum toxoid The authors concluded that from a public health viewpoint the single dose had produced immunity for 28 months in a satisfactory percentage of individuals.

The reactions produced by injections of diphtheria toxoid differ in various individuals and it is advantageous to know which persons are especially susceptible C. R. Hayman^{6,2} compared the reactions of 289 persons of various ages to the Schick test and to the intracutaneous inoculation of diluted toxoid (Moloney test). About 15 per cent of the group had systemic reactions following the injection of the toxoid and the frequency of these reactions was 3 times greater in the individuals over 15

years of age than in younger age groups. Patients with positive Moloney tests and older aged children who had positive control Schick reactions developed untoward symptoms more frequently than the remainder of the group. As a rule, the patients who received small amounts of the toxoid for immunizing purposes developed reactions more frequently than those who received larger amounts, so that large dosage did not seem to cause unfavorable symptoms. Reactions could not be eliminated by drastic reductions in dosage. In certain individuals, however, serial injections of increasing potency tended to produce respectively larger and more frequent reactions. It was the conclusion of the author that the increasing age of the patient and the positive cutaneous reaction to the diluted toxoid material were the best indications that reactions to the immunizing agent might occur.

The necessity for repeating Schick tests or the immunizing inoculations has been emphasized by C H Maxwell. B L Cullen and R J Thomas 63 During a small epidemic of the disease in a school, the immunity of the pupils was retested and 88 per cent of a group of 319 young children who had been immunized previously were still negative. Of the positive group, however, there were 13 per cent who had been negative previously and had reverted to positive zones. In high school groups the percentage of positive reactors was not high but 43 per cent of this latter group had once had negative reactions. The same general condition was true in a group of nurses. Recent experience with throat cultures of groups of children has indicated that positive results were rarely noted in children except those who had the disease or who had been directly exposed to the infection The maintenance of immunity levels of antitoxin in

all children can only be obtained by the repeated Schick testing at intervals of at least 7 years and the administration of the antigen to susceptible patients

Scratch tests for the determination of immunity to diphtheria were employed in a series of 100 children by M. Grozin. 64 The test material was composed of a toxin which contained 1200 minimal lethal doses per cubic centimeter. A drop of this was placed upon the arm and slight scarification was made with a stylet. The reaction reached its height between the second and fourth days When the results of this scratch method were compared with those of the standard Schick technic, complete agreement between the 2 tests was noted in 92 per cent of cases. In the 8 per cent of patients in whom there was some difference between the 2 tests, it was generally the Schick reaction which was negative and the scratch test which was positive. The reactions to the scratch test seemed to be specific for diphtheria. The advantages of this technic over the intracutaneous method were the elimination of syringes and needles and the greater simplicity and rapidity of performing the test

Combined diphtheria and tetanus toxoid material has been administered to a group of young adults by F. G. Jones and J. M. Moss, 65 and the blood antitoxin titers observed over a period of years. Two doses seemed to be adequate to establish satisfactory immunity levels and neither toxoid inhibited the development of antitoxin to the other Intervals of 2 to 3 months between the

injections seemed to produce a maximum response to the antigens. The antitoxin of either disease could be raised rapidly to very high levels 6 months later by another injection of the specific toxoid, or in the case of diphtheria by a Schick test alone. The immunity gained by these secondary injections of toxoid persisted over a year's time with higher antitoxin values than those obtained after the initial pair of injections. The decreases of quantities of antitoxin also took place at slower rates following the stimulating injection than after the original treatment.

The experiments of D H. Bergey, C. P. Brown and S Etris⁶⁶ indicated that 2 or more injections of the tetanus toxoid are necessary to establish protective levels of antitoxin in the blood. In 2 groups of adults, the first injection stimulated the production of very small amounts of the antitoxin but the second dose increased the antitoxin content 100 to 500 times. In their judgment, 0.01 unit of antitoxin in the blood was adequate for protection against the disease although the resistance of experimental animals to the infection was found to be much greater than the quantity of blood antitoxin would indicate Examination of the patients 1 to $1\frac{1}{2}$ years after the second dose of toxoid showed that the antitoxin in the blood had diminished to about one-fifth of its former level and there was a probability that a repetition of the treatment would be necessary at fairly frequent intervals if it was desirable to increase the immunity

ENDOCRINE DISTURBANCES

By Josef Warkany, M D.

Adrenals

W. O. Thompson, P. K. Thompson, S. G. Taylor, III, and W. S. Hoffman⁶⁷

discuss the use of adrenal cortex extract in the treatment of Addison's disease, the extract of the Wilson Laboratories, each cc. of which represents 75 Gm. of fresh beef adrenal, was used in this study. It was found that from 10 to 20 cc. daily will often maintain life for long periods without any other form of therapy, but larger amounts are probably necessary to produce optimum conditions.

In a crisis, it is important to begin treatment at once, as delay may be fatal. Ten cc. of an active adrenal cortex extract and about 170 cc. of 5 per cent dextrose in normal salt solution should be administered intravenously until vomiting stops and appetite returns. There is no danger of giving an overdose.

Early in a crisis a patient may be revived by extract alone When a crisis is well advanced, extract alone is not effective, presumably because of depletion of the sodium reserves of the body.

Following recovery from a crisis, patients may be maintained by administration of an active adrenal cortex extract in an adequate dose (at least 10 cc. daily), and by administration of about 12 Gm of sodium chloride and 4 Gm. of sodium citrate or bicarbonate daily by mouth A diet high in Calories and low in potassium should always be given.

An adequate dose of the extract appears to produce a more satisfactory clinical condition than sodium salts alone Because of expense, however, it may sometimes become necessary to hold the extract in reserve for crises and patients can be maintained by sodium salts.

The dose of the extract should be increased during an infection. If no active tuberculous infection is present, patients may be maintained in a satisfactory condition for long periods. There appears to be some relationship between the nutritional state of the patient and the level of the blood pressure. When the basal metabolism is low, raising it to

normal with a suitable dose of thyroid is an important part of the treatment. Under such circumstances no aggravation of the disease from the use of thyroid has been observed.

Gonads

A study of hypergenitalism in children has been made by I. P. Bronstein.⁶⁸ A case is recorded of a mentally retarded boy, 9½ years of age, with precocious sexual development exhibiting neither spermatogenesis, premature ossification, nor precocious epiphyseal union. Hydrocephalus was not present.

W. O. Thompson and N. J. Heckel⁶⁹ warn against the indiscriminate use of anterior pituitarylike hormone in patients with undescended testes. Changes simulating premature puberty have been produced in 3 boys, 4, 7, and 9 years old, by the administration of the anterior pituitarylike principle from the urine of pregnant women. These changes consisted of an increase in the size of the penis, scrotum, and prostate, increased masculinity, a growth of pubic hair and a change in the pitch of the voice. In contrast to the marked growth of other parts of the genitalia, the testes showed very little change in size

Some genital growth has been produced with this material in 16 of 33 patients with undescended testes; and in 14 patients, including 2 of the 3 boys who developed changes simulating premature puberty, it was marked. However, descent was produced in only 23 per cent of the total number of undescended testes, showing that genital growth may occur without descent of the testis.

The treatment for undescended testes with the anterior pituitarylike principle should be stopped before genital growth becomes marked According to these authors, if this rule is followed, it

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would appear that in the present state of our knowledge its routine use is justifiable and desirable.

W. Saphir, K. M. Howell and R. H. Kunstadter⁷⁰ examined the human serum response to gonadotrophic hormone (pregnancy urine extract). Sera of human beings receiving large doses of gonadotrophic hormone (pregnancy urine extract) were examined for the presence of antihormones and for complement fixation antibodies.

Injection of the human sera into mature and immature female white mice over a prolonged period of time did not produce any noticeable changes upon the normal estrus cycle or histologic changes in the ovaries. Injection of the sera into infantile female rats failed to inhibit the gonadotrophic response produced by injection of antuitrin-S. Antuitrin-S injected into patients elicited a thermolabile factor in their sera that fixed complement in the presence of antuitrin-S antigen (pregnancy urine extract) and in the presence of an extract of normal urine used as antigen.

It is concluded from this study that human beings do not respond with either true antibody or antihormone formation following the injection of gonadotrophic hormone

The rôle of gonadotrophic hormone in the surgical treatment of cryptorchidism is discussed by J. A. Bigler, L. M. Hardy and H. V. Scott ⁷¹. In children with cryptorchidism requiring surgical repair, slightly better results were obtained when a gonadotrophic substance was given before operation than when operation alone was resorted to

Postoperative treatment with a gonadotrophic principle had no beneficial effects on the testes which had been operated upon, either in preventing or in correcting atrophy The best results seemed to occur between the ages of 7 and 10 years with all forms of treatment. According to these authors, the gonadotrophic principle should be tried in the treatment of cryptorchidism in boys over 7 years of age, before operation is considered.

The treatment of hypogonadism in the adolescent male was made the subject of a study by B. Webster. By the use of testosterone propionate in 6 cases of adolescent hypogonadism striking anatomical changes resulting in the growth of the penis, scrotum, and prostate were obtained. Secondary sexual characteristics such as growth of the hair and change of the voice occur as in the normal process of puberty. It seems that this substance offers a means of inducing, in hypogonadal adolescent males, the anatomical changes which normally occur at puberty.

Fifty-four patients with various types of genital anomalies and dysfunctions, which included adult hypogonadism, sexual diminution associated with senescence, adiposogenitalism, gynecomastia, and benign prostatic hypertrophy were treated with the synthetic male sex hormone, testosterone propionate, in a study made by H. Turner.⁷³ In doses of ½ to ½ grains (10 to 75 mg.) weekly, it was found effective in every hypogonad case and no untoward by effects were noted in any of the cases treated

The treatment of testicular deficiency with testosterone propionate has been studied by E P McCullagh 74 In cases of severe prepuberal hypogonadism, injections of testosterone propionate have been followed by symptomatic and anatomic changes in approximately the following order: Penile erections occur promptly, and there is an increase in the pubic and axillary hair. The penis grows rather markedly and the scrotum less so, and the prostate growth appears to lag

perceptibly in proportion. There has been no consistent evidence of increased testicular size, although the testes appeared to be larger after treatment in 1 case. Nocturnal emissions occur and the quantity of semen increases. No diminution in sperm count or inhibition of sperm production has been obvious where sperms are present, though this may not be so in cases in which there is a normal number of spermatozoa before therapy. The larynx grows and the voice becomes lower. Facial acne appears and the beard grows. Epiphyseal closure has not exceeded its expected normal rate in cases in which testosterone propionate alone was used and in 1 case has not increased in 4 years in spite of marked advance in puberty. No constant change in basal metabolism has been observed. In cases of functional hypogonadism in the adult this treatment has been followed by complete relief of nervous and sexual symptoms In castrates, nervous and vasomotor symptoms and impotence can be abolished by sufficient doses

The induction of premature puberty with androgenic substance was observed by R H Kunstadter⁷⁵ in 2 sexually retarded boys, aged 1112 years and $10\frac{2}{3}$ years, respectively, by the intramuscular administration of testosterone propionate. In addition to the establishment of premature puberty in the case of the older boy, abnormal genital hypertrophy resulted At the onset of treatment both boys presented small genitalia which were not considered dystrophic In view of the results obtained in these 2 patients, the author emphasizes the danger of administering potent androgenic substance to young individuals

It may be gathered from these studies that the use of androgens should be restricted to persons with hypogonadism and preferably to adults.

Parathyroid

Two cases of osteodystrophia fibrosa were reported by P. Summerfeldt and A. Brown.⁷⁶ A girl 6 years and one 10 years of age exhibited precocious puberty, yellow pigmentation of the skin and osteodystrophy, the last progressing to cystic formation which resulted in fractures and skeletal deformity. There were increase in the basal metabolic rate. and in the blood pressure, disturbance in the lipoid metabolism and decrease in carbohydrate tolerance. The authors considered a disturbance of the lipoid metabolism as an etiologic factor, but the microscopic examination of bone, obtained by biopsy, showed no foam cells in sections stained with hematoxylin and eosin or with scarlet red; doubly refractile bodies could not be demonstrated by the use of crossed Nicol prisms.

Tetany in newborn infants was analyzed in a study by H. Bakwin 77 He concludes that a physiologic hypoparathyroidism occurs in newborn infants analogous to physiologic dehydration and physiological jaundice. That the tetany of newborn infants results from hypoparathyroidism is indicated by the abrupt fall in serum calcium within 24 hours after birth, the low urinary phosphorous content, and the marked response to phosphate ingestion. That tetany in the newborn is not related to vitamin D deficiency is indicated by the failure of large doses of vitamin D to influence the fall in serum calcium following phosphate ingestion and the prompt cure with calcium salts.

A second mechanism leading to tetany of the newborn is an increase of phosphates, either released endogenously during the physiologic starvation, or ingested from without in cow's milk.

In this connection a thorough discussion of the regulation of the level of calcium in the serum during pregnancy seems of great interest. M. Bodansky and V. B. Duff⁷⁸ review this subject, taking into consideration all the factors known to be involved in the maintenance of a stable calcium level. Dilution of blood, protein concentration of the serum, parathyroid and other hormonal influences, calcium intake and seasonal variations are considered separately. The authors conclude that within certain limits (not lower than 8.5 mg.) the depression of calcium in the serum observed in late pregnancy may be considered a normal condition.

Severe hypocalcemia during pregnancy may reflect either parathyroid deficiency or marked nutritional deficiency. Both are comparatively rare in ordinary clinical experience.

Abnormalities in fetal skeletal development occur if hypocalcemia is severe, as shown by the results in experimental parathyroid deficiency and in clinical osteomalacia. The somewhat elevated calcium level in the fetal circulation may therefore be looked on as normal for fetal development. Nutritional, hormonic and seasonal factors influence the maternal calcium level.

It is possible that in pregnancy the maintenance of a subnormal calcium level in the maternal serum is dependent on an intrinsic calcium-depressing factor The maintenance of a relative elevation of calcium in the fetal serum may also indicate the participation of some factor in the fetal organism independent of the fetal parathyroid glands. The rise in the maternal calcium level after parturition and the decline in that of the newborn infant suggest that these factors may reside in the maternal and fetal portions of the placenta respectively. each playing a distinct and important rôle in the regulation of the maternal and the fetal calcium level. The decline

in calcium content observed in the newborn may also be conditioned by the sudden withdrawal of the labile calcium reserve of the fetal placenta.

Pituitary

Since the interrelationship between the hypothalamus and the hypophysis has become of increasing interest to the clinician, a thorough study of the innervation of the human pituitary gland seems of great importance. A. T. Rasmussen's work⁷⁹ is based on the study of 48 human hypophyses, prepared by selective silver methods. The results are summarized by the author as follows:

"There are at least 50,000 fine unmyelinated nerve fibers descending from the hypothalamus into the infundibulum, and there are that many cells in 1 supraoptic nucleus. This relatively enormous nerve supply appears to be all out of proportion to the cellular content of the neural lobe, and to the amount of epithelium in pars tuberalis, pars infundibularis and pars intermedia.

"The density of nerve fibers in processus infundibuli (posterior or neural lobe in a narrow sense) renders it virtually impossible to rule out by morphological means the possibility of nerve contacts with the cells in its meshes. However, these cells have never been proven to be secretory, and the nerves may function through a humoral mechanism rather than by direct activation of secretory cells.

"Only an occasional nerve fiber is seen among the epithelial cells of pars tuberalis and pars intundibularis (the jacket of cells along the infundibular stem).

"Large areas of pars intermedia apparently may be devoid of nerve fibers, whereas in other places, especially where it is represented by basophilic cells that invaded the neural lobe, there may be a rich plexus of nerve fibers between many of the epithelial cells, but this evidently is a case of epithelial cells having grown into a nerve plexus and hence of no primary importance. Many of the nerve fibers encountered in pars intermedia appear to be there only incidentally. There are a number of structures that suggest nerve terminals on the cells of pars intermedia. Many of these are apparent rather than real. A few cannot be thus disposed of.

"A few nerve fibers pass from the neural lobe through the intermediate region and get slightly into pars distalis (anterior lobe), but the number is negligible.

"There are numerous small unmyelinated nerves in the connective tissue capsule of the hypophysis. They are most conspicuous on the upper surface of the anterior lobe. They are derived from the cavernous sympathetic plexus and probably represent about 200 fibers. A few of these ascend along the blood vessels of the stalk A conspicuous number pass into and along the vascular stroma anteriorly and laterally in the upper superficial part of the anterior lobe A few individual fibers ultimately ramify among the epithelial cells

"A large right and a left group of fibers, commencing just lateral to the stalk, descend deeply into the corresponding half of the anterior lobe, where they usually become associated with prominent blood vessels. Some of these fibers disseminate themselves among the gland cells of a limited region deep in the anterior lobe

"Several small capsular nerves pass downward and forward, sending a few fibers into the substance of the anterior lobe at numerous points. The larger strands are usually near arteries or veins. Individual fibers from this source intertwine among the glands cells, but rarely penetrate very far into the lobe. No definite nerve terminals were seen strictly in the anterior lobe. Some of the capsular fibers have been followed along blood vessels into the neural lobe where they become lost in the dense nervous plexus.

"Such a large proportion of the anterior lobe appears to be so devoid of nerve fibers that secretory nerves to this part of the hypophysis remain highly questionable. The nerve fibers in this lobe are most likely connected with the vascular system"

An interesting experimental study on growth hormone and the localization of its point of attack was made by J. Freud, L. H. Levie and D. B. Kroon ⁸⁰ Using growth of the tail in rats as a test object these authors found that after hypophysectomy, longitudinal bone growth ceases, and 7 days after operation the difference between operated and control animals may be readily detected in skiagrams. The epiphyses are closed soon after

hypophysectomy. Epiphyseal closure, once completed, cannot be reversed by treatment with growth hormone. Growth hormone treatment, when commenced immediately after hypophysectomy, prevents epiphyseal closure and maintains normal longitudinal growth in the tail.

The assay of growth hormone is simple and reliable, using as indicator the tail length and vertebral development as shown by serial skiagrams. A minimal requirement of 6 mm. growth is advised as a basis of comparison between unknown and reference standard preparations. The growth defect after hypophysectomy is definitely localized in the growing epiphyseal cartilage.

The histological features of the process of growth cessation after hypophysectomy are exactly analogous to those exhibited at the end of the normal growth period

Growth hormone has a biologically typical point of attack at the proliferating cartilage and the terms growth hormone and chondrotrophic hormone are therefore synonymous.

A A Werner⁸¹ observed severe reactions from the use of lactogenic hormone Local reactions, such as redness, induration and soreness, and generalized reactions like edema, difficulty in respiration and swallowing, and intense itching, followed the injection of lactogenic hormone The author concludes that the present preparations of lactogenic hormones are impure and unsafe for human

A critical review of etiology, diagnosis and treatment of diabetes insipidus was made by J. Warkany and A. G. Mitchell ⁸². The difference between symptomatic and etiologic treatment is pointed out. Since definite progress has recently been made in the understanding of some of the etiologic processes underlying this condition, its classification as well as the

evaluation of its symptomatology was reconsidered. The following etiologic classification of diabetes insipidus was suggested:

- 1. Idiopathic-hereditary
- 2. Due to trauma
- 3. Due to encephalitis
- 4. Due to tuberculosis
- 5. Due to syphilis
- 6. Due to xanthomatosis
- 7. Due to tumor
- 8. Due to rare etiologic factors
- 9. Unclassified.

The underlying pathologic process responsible for diabetes insipidus is in some instances susceptible to treatment. This may obtain in cases of syphilis, xanthomatosis, tumor of the brain, traumatic lesions, pellagra and some forms of hydrocephalus. Spinal puncture may have its indications. Symptomatic treatment consists largely of the use of extract of the posterior lobe of the pituitary gland (preferably pitressin) administered by injection or intranasally. A number of other substances and drugs has been advised from time to time. Four case reports of children showing diabetes insipidus are added to this review

Thymus

The problem of the thymus in children was discussed by A. G. Mitchell and J. Warkany.⁸³ There are 3 ways in which the pediatrician may encounter the problem of the thymus They are the questions of thymic hyperplasia, status thymicolymphaticus and the rôle of the thymus as an endocrine organ

As to the first question, anatomic and clinical observations support the view that an enlarged thymus gland may occasionally cause such symptoms of compression as stridor, dyspnea, cyanosis, and dysphagia. These occur also in many other abnormal conditions, which are

more frequently operative in their causation than is disorder of the thymus. Radiologic treatment, carefully given in proper dosage, is a justifiable procedure when the thymus gland is suspected as the cause of such symptoms and when no other cause can be found. If the thymus is responsible or partly responsible for them, they should be relieved by from 1 to 3 such irradiations.

If such a condition as status thymicolymphaticus exists, and if it is in any way related to sudden death, there is no justification for the belief that radiologic treatment or extirpation of the thymus or administration of thymus extracts would have prevented such death. Abnormalities of the thymus could only be part of such a syndrome.

An effect of antuitrin-S on the thymus of the young albino rat has been observed by E. O. Butcher and E. C. Persike, Jr 84 Injections of the gonadotrophic hormone, antuitrin-S, causes arrested growth of the thymus in young albino rats. This effect has not been induced before the eighteenth day, and is the gonads, since no effect can be induced in gonadectomized animals. Effectiveness declines in the female with continued injections. The changes induced in the thymus have no effect on the body growth of the animal.

Thyroid

O. P. Kimball⁸⁵ tells how the prevention of goiter, based upon the researches of David Marine and his associates, was started in the public schools of Akron by giving large doses of sodium iodide Two Gm. of sodium iodide were given twice yearly. The results were very satisfactory and not a single case of hyperthyroidism was observed in spite of the large doses. The example of Akron was followed by the schools of Switzerland and many other countries After Hay-

hurst pointed out that previously common table salt had been the chief source of iodine and that the present-day methods of refining probably played an important rôle in the production of goiter, the use of iodized salt was commenced. At the present time iodized salt in this country is standardized so that an individual using the average amount of salt will get 400 mg. of iodine per year. The percentage is 0 02 if sodium iodide is used and 0.023 if potassium iodide is used. This iodine content is very high if compared to the iodine contained in iodized salt used in Switzerland. The author summarizes his opinions and recommendations as follows:

- "1 Simple or endemic goiter is a deficiency disease and this deficiency is iodine in our food and drink. This iodine deficiency was caused primarily by geological conditions and has been made worse by our refinement of foods such as salt.
- "2. The addition of an exceedingly small amount of iodine to our food in endemic goiter regions prevents goiter. The most practical method yet devised is iodized salt
- "3 There is no basis for the old teaching that the general or so-called indiscriminate use of iodine in amounts sufficient to prevent goiter might have some injurious effects
- "4 In the prevention of endemic goiter we prevent adenomas and toxic goiters, cretinism and cretinoid type of subnormal mentality, deafmutism, congenital malformations and many cases of infantilism in girls or a relative subnormal development
- "5 There is no contraindication to the amount of iodine used in iodized salt in this country. Judging from the observations of Dr. Hans Eggenberger throughout Herisau, Switzerland, we are obtaining better results in America than they are getting in Switzerland with the iodine content of their standard salt only one-tenth of our iodized salt. At the International Meeting in Washington, D. C., September, 1938, Dr. Eggenberger proposed to the American Association for the Study of Goiter that this Association go on record in favor of the prevention of goiter in America by the use of iodized salt. This proposition was unanimously adopted. In November of

1938 the advisory council of the American Medical Association on foods and drugs recommended that iodized salt, .01 per cent (1:10000) be used wherever goiter is endemic.

"6. In each state where goiter is endemic and iodized salt is used, the State Department of Health should recheck the iodine content of each brand yearly and thereby maintain a set standard throughout this country. Then, endemic goiter with all of its manifestations will have been eliminated."

A study of the factors influencing appearance of centers of ossification during early childhood was made by C. C. Francis. So This study deserves attention chiefly since 1 of the factors—the rôle of the thyroid—has been overrated in recent years. The author found the sequence as well as the date of appearance for centers of ossification rather regular; however, they may be interrupted or retarded by metabolic or constitutional disturbance

Epiphyseal rating is an early and frequently the only indicator of such a disturbance. The progress in epiphyseal rating may be used as a rather delicate measure of constitutional health in young children, but it cannot be employed as an indicator of bodily maturation. Sick children show a lag in epiphyseal rating proportionate to the duration and intensity of the disturbance. The epiphyseal rating advances again when convalescence is completed

One of the factors which influence epiphyseal rating is the availability of minerals and vitamin D. Children on a low mineral ration tend to lag in epiphyseal rating, and children growing very rapidly will tend to lag in epiphyseal rating unless they are provided with ample rations of mineral and of vitamin D. When the period of rapid growth comes to a close, the epiphyseal rating advances rapidly. Children growing slowly and given a diet rich in mineral and vitamins, particularly vitamin D.

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tend to advance rapidly in epiphyseal rating.

The influence of thyroid therapy on mental growth of cretins was studied by A. W. Brown, I. P. Bronstein and R. Kraines.⁸⁷ The authors studied 29 cretins and 4 cases of hypothyroidism, all of whom were treated with thyroid preparations. Psychological tests were given over a period of from 1 to 7 years to determine the mental development of these children. The following interesting conclusions were reached by these authors:

- "1. Cretins if treated are not all predestined to a fixed low mental age A small proportion of them may develop normally
- "2. There is evidence that early recognition of the abnormal condition and active and persistent treatment thereafter are the important factors in producing ultimate mental development

"There are a number of factors which may account for the failure of some children to respond to treatment even though it is initiated early

"In general, there was a slight increase in the intelligence quotient during the period of treatment since referral to the clinic. The increase was greatest for those who began treatment early.

"Even with treatment, most of the children remained severely retarded, having intelligence quotients below 70. The chances are that at maturity their mental level will not be much above 10 or 11 years

There is no evidence from our data that cretins have any special aptitudes or abilities. The retardation seemed general

"When on successive examinations mental ages were plotted in Heinis mental growth units, the curve seemed to have the same general shape as the curve for the average child except that they were at a lower level

"Examination of a number of the siblings indicated that the cretins did not come from families of low intellectual status

"In a study of 13 cretins there appeared to be some relation between development of carpal bones and mental age"

A study of the basal metabolic rate in children with abnormal bodily dimen-

sions was made by M. de Bruin.⁸⁸ The basal metabolic rates were estimated by means of the apparatus of Dusser de Barenne and Burger in 120 normal boys and 123 normal girls. On the basis of the figures obtained, standard curves for normal children were made and the rates calculated according to the weight.

By the same method, the basal metabolic rates were determined for 107 children with abnormal bodily dimensions. The investigation included 13 fat boys, 22 fat girls, 6 thin boys and 10 thin girls. Besides, measurements were done on 56 children who were too tall or too short for their age but otherwise normally proportioned. These were divided as follows 10 tall boys; 1 tall girl, 14 short boys and 31 short girls. With the aid of the results, an attempt was made to draw up standards for determining the basal metabolic rates of children of abnormal size The following mode of calculation is proposed by the author:

- "1 For a fat boy with an excess of weight up to 35 per cent, the rate is based on the actual weight, with a greater excess of weight, on the standard weight for the actual height, increased by one-third of the excess over the standard weight
- "2 For a fat girl with an excess of weight up to 20 per cent, the rate is based on the actual weight; with a greater excess of weight, on the standard weight for the actual height, increased by one-third of the excess over the standard weight
- "3 For a thin boy or a thin girl, the rate is based on the actual weight
- "4 For a well proportioned child who is too tall or too small for his age, the rate is based on the actual weight"

Basal metabolic rates of 8 children with the nephrotic syndrome were measured by L E. Farr.⁸⁹ In none was a consistently lowered basal metabolic rate found, using the standards of Lewis, Kinsman and Iliff. In 1 case, a slightly but consistently elevated rate was noted

The basal metabolism of undernourished girls was studied by F. B. Talbot. 90 This author and his co-workers 91 have previously published standards for predicting the heat production of children, which differ from those commonly in use. The author's present study of undernutrition is based on the premise that the body is composed of 2 main types of tissue. The 1 which is called active tissue includes muscles and possibly organs. The second, called inactive tissue, includes bone, water and fatty tissue. The results of this study are summarized by the author as follows:

- "1. During acute undernutrition there are a rapid loss of weight and a corresponding lowering of the heat production.
- "2 Severe chronic undernutrition is associated with a lowered production of heat. The greater the degree of malnutrition the less the heat production of the body.
- "3 The teaching that malnutrition is accompanied by increased heat production resulted from the error of using standards for metabolism which divide the total amount of heat produced by body weight, or by body surface when weight is used in the formula. Results obtained with such standards are only relative and do not give evidence of the true physiologic status
- "4. The heat production of girls who are between 10 and 20 per cent below their normal weight averages 7.2 per cent less than the total calories for the expected weight as shown by the height standard. With more severe malnutrition the heat production averages 10.4 per cent less than the total calories for the expected weight and may be as low as —27 per cent below that value.
- "5 Even though the absolute heat production is diminished, it may appear to be increased if there is a greater proportional loss in inert tissues than in heat production. When standards are based on body weight, as is the case with body surface standards and the 'multiple prediction formula,' the metabolism will appear to be increased or diminished according to the composition of the weight lost. In order to obtain a knowledge of the true state of affairs in malnutrition, the absolute total heat production should be compared with standards ex-

pressed in the terms of expected average weight for the height. This can be done simply by using the height standards"

Since a relation between basal metabolism and the urinary output of preformed and total creatmine has been asserted, a study by C. C. Wang⁹² on the basal metabolism and preformed and total creatinine in the urine of 70 children appears of interest. The result of this extensive study is presented here by the summary of the author:

- "1 Under the age of 5 years the 24-hour values for basal heat production of 70 children increased much more rapidly than those for the preformed creatinine nitrogen output Between the ages of 5 and 11 the increase for preformed creatinine nitrogen output exceeded that for basal metabolic rate Thereafter the 2 curves ran nearly parallel until about the age of 14 years, when the rate of rise of the preformed creatinine nitrogen output again exceeded that of the basal metabolic rate.
- "2 Beginning at the age of approximately 6 months, the per kilogram values of the basal metabolism declined slowly and steadily throughout childhood, while those of the preformed creatinine level increased steadily until about the age of 10 years, when they began to approach constancy
- "3 Basal metabolism expressed in terms of calories per milligram of preformed urinary creatinine nitrogen followed a course similar to that of calories per kilogram of body weight
- "4 Values for total creatinine followed the same trend as those for preformed creatinine, except that they were less consistent
- "5 With the exception of the values for basal metabolism expressed in terms of calories per milligram of preformed and total creatinine nitrogen output, the correlation coefficients of which were all negative, the coefficients of correlation of all factors studied were positive and unusually high. The preformed creatinine nitrogen output was most closely correlated with body weight and least with basal metabolism expressed as total calories per 24 hours, which was most closely correlated with height
- "6 Except for the girls of the 13-year-old group, for whom the preformed and the total creatinine values were higher and those for basal metabolism in terms of calories per milligram of preformed creatinine were lower, sex

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had no demonstrable influence on the total per 24-hour values. With a few exceptions, the per kilogram values of all factors tended to be lower for girls than the corresponding values for boys.

"7. Owing to the facts that the basal metabolic rate and the preformed creatinine content did not run parallel at all ages for this group of children, that the ratio between the 2 was not constant and that the values in the present study varied considerably from those reported by Talbot, it is suggested that some other factor or factors aside from active protoplasmic tissues may be responsible for production of either basal heat or creatinine or of both and that more work is therefore necessary before preformed creatinine values can be safely employed as a standard for basal metabolism"

GENITOURINARY SYSTEM

By Waldo E. Nelson

Kidney Function Tests

Experiments designed to determine whether inulin may be secreted by the renal tubules have been carried out by A. N. Richards, P. A. Bott and B. B. Westfall 93 In the first experiment inulin was perfused through the renal portal vessels of the frog's kidney, none gained access to the lumen unless the tubule had been subjected to injury. It was thus shown that mulin was not secreted by the frog's tubule experiments were performed with dogs and rabbits in which filtration in the kidney was temporarily abolished by lowering the renal blood pressure. Inulm, along with other substances known to be secreted (phenol red, diodrast, hippuran) was contained in the blood circulating through the kidney during this period. Urine, subsequently obtained, contained enough of the secretable substances to prove the secreting power of the tubules had not been abolished, it contained so little inulin that the conclusion was warranted that the tubules in dogs and rabbits are not capable of secreting that substance experiments strengthen the belief that the glomerulus is the sole pathway of secretion of inulin in normal animals

The main disadvantage of the Addis sediment count of the urine as a kidney

function test is that it requires much time, the labor entailed restricting its usefulness in clinical work. For this reason J. K. Calvin and J. Carbone⁹⁴ recommend the orthotolidine test for the determination of erythrocytes in urinary sediment This is a rapidly performed, accurate test, for determining the limits between normal and pathologic numbers of erythrocytes in urmary sediment. It is stated that the reaction to the orthotolidine test becomes faintly positive in the centrifuged urinary sediment when there are 250,000 erythrocytes per 500 cc of fluid. It was found that the concentrated urinary sediment of the great majority of healthy children tested gave a negative orthotolidine reaction contrast, abnormal numbers of erythrocytes were found at some time during the second, third, or fourth week in 99 of 202 children who were convalescing normally from scarlet fever

The author suggests that the orthotolidine test may be used in office, hospital and clinical practice in place of the Addis count for the wider studies of the following clinical problems (1) The incidence and duration of subclinical nephritis following minor infections, such as colds and more throats, as well as after more severe streptococcic infections, such as tonsillitis and scarlet fever; (2) the incidence and duration of latent nephritis following acute clinical glomerulonephritis and the complete healing of the kidneys in these cases; (3) the missing link (latent nephritis) between the acute and the chronic stages of glomerulonephritis by examining patients who have "recovered" from acute nephritis at intervals of 6 months to a year for many years; (4) the more accurate differentiation between chronic glomerulonephritis during the nephrotic stage and true nephrosis, and (5) the determination of the effects of various kinds of therapy on the course of glomerulonephritis.

Orthotolidine Test—The technic of the orthotolidine test is as follows:

"The urine is collected as for an Addis count When this test is done with children, fluid is withheld during the afternoon and night except for 200 cc given at an early evening meal, a sample of urine collected between 7 PM and 7 A. M. will usually contain about 400 cc. of urine with a hydrogen ion concentration between 5 and 6 and a specific gravity well above 1020 The urine is sufficiently acid and concentrated that most of the red cells will not disintegrate. The concentrated night urine is thoroughly shaken and mixed.

"According to Stone and Burke, the test is performed as follows:

- "1 Orthotolidine 1 per cent in chemically pure methyl alcohol (It dissolves with slight difficulty and keeps at least 10 months.)
- "2. Glacial acetic acid 1 part and commercial hydrogen peroxide 2 parts. (This keeps for 3 or 4 months, probably longer.)
- "3. Fifteen cc. of urine are centrifugated at about 1500 revolutions per minute for 5 minutes. The supernatant fluid is poured off. A portion of the sediment is prepared for microscopic examination in the usual way. To the

remaining sediment 2 drops of the orthotolidine solution is added plus 2 or 3 drops of the acid-peroxide solution. In the presence of blood cells aggregating 100 per cubic millimeter of sediment (approximately 1350 per cubic centimeter of urine) a greenish blue color develops, lasting about 1 minute. In the presence of from 300 to 500 red cells per cubic millimeter of sediment (approximately 4000 to 6500 cells per cubic centimeter of urine) a deeper blue color develops lasting about 1 minute. the presence of larger numbers of red cells, aggregating 1000 per cubic millimeter of sediment (approximately 13,000 per cubic centimeter of urine) as in hemorrhagic Bright's disease (glomerulonephritis) a deep blue color develops lasting 2 minutes or longer.

"Undiluted blood serum, 10 per cent sodium hydroxide, strong trisodium phosphate solutions and probably other strong alkalis will give positive reactions. Pus cells or any of the common organic or inorganic constituents found in the urine do not give positive reactions. Iodides and bromides eliminated in the urine may at times cause a confusing blue-black color The erythrocytes in specimens of urine containing as high as 5000 red cells per cubic centimeter will in most instances be undetected by the usual microscopic examinations, since such numbers may represent only 1 or 2 cells per high power field

"The color change is so sensitive that once a strongly positive reaction has been obtained in a glass centrifuge or test tube the container must be thoroughly washed and scrubbed with soap and water a number of times before the drops of wash water collecting at the bottom and sides will not give a bluish color when the reagents are again added. All the glass apparatus to be used, especially after a positive reaction has been

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obtained must first be tested with the reagents before the apparatus is used again in order that one may be certain that no bluish color will develop."

Nephritis

Hemorrhagic Nephritis - Studies which are designed to accumulate more specific evidence concerning the character of the infection which precedes acute glomerulonephritis are being conducted by J. D. Lyttle, D. Seegal, E N. Loeb and E. L. Jost.⁹⁵ There is general agreement that the antistreptolysin level in persons who have been free of hemolytic streptococcus infections is less than 100 units. Most workers, with some exceptions, also agree that the antistreptolysin titer rises following infection with the hemolytic streptococcus and that high titers may be maintained for some time after the infection has subsided The rise in titer may be moderate in degree and of brief duration, and may be shown only when determinations are made for a period before and after an infection in order to obtain the natural or base level. The authors have considered an antistreptolysin titer of 125 units or more as an evidence of recent infection with hemolytic streptococcus if previous or subsequent determinations had shown the level to be lower.

In 116 consecutive cases of acute glomerulonephritis, the bacteriologic data indicated that 71.5 per cent had had a prodromal hemolytic streptoccal infection and the immunologic data showed that 94 per cent had had a recent hemolytic streptococcal infection. The height and duration of the antistreptolysin titer in the patients with acute glomerulonephritis appeared to be related to the severity, persistence, or recurrence of the hemolytic streptococcal infection. On the other hand, analysis of the immunologic and clinical data in this study

did not show any significant correlation between the height and duration of the antistreptolysin response and the severity or duration of the acute attack of nephritis or the tendency to develop chronic nephritis.

A. W. Snoke carried out studies on 2 groups of children who had had acute hemorrhagic nephritis. The differences in the 2 groups are illustrated in Tables 3 and 4. It was found that a much higher percentage of children recovered from glomerulonephritis in the Rochester group. These differences are not adequately explained, but the possibilities are suggested that differences may result merely from chance selection of cases or possibly from a geographic difference in the clinical manifestations of glomerulonephritis.

Complete recovery from acute glomerulonephritis in patients under 20 years of age is reported in 50 per cent of a series of cases by F. D. Murphy and J W Rastetter ⁹⁷ In approximately 40 per cent of instances, chronic nephritis developed and approximately 10 per cent died This low recovery rate corresponds with that previously reported by Snoke In agreement with Snoke, these authors also believe there is no relation between the severity of the initial attack and the development of chronic nephritis They point out that mild forms of nephritis are frequently overlooked in the acute stage, and evidence of renal damage is not observed until the disease has progressed into the chronic stage and renal insufficiency is present. They state that if success in the treatment of acute nephritis is to be achieved, prompt recognition of the early and mild types is of the first importance After the manifest symptoms of acute nephritis have subsided, there is a period called the transitional stage in which the renal lesion may heal completely or the disease may

TABLE 3						
GLOMERULAR	Nephritis	\mathbf{With}	History	OF	Initial	Stage

			Rochester		Stanford	
			Number	Percentage	Number	Percentage
Lesions healed			76	<i>7</i> 4.5	44	40
Lesions active			14	137	52	47 2
Patient dead			12	11 8	14	12.8
Case not followed			39		20	•
					*	
Total	•		141		130	

(Snoke Am J Dis Child.)

progress into the subacute or chronic form. It is necessary to determine whether or not healing has occurred. They do not believe that any one test will give this information, and a combination of diagnostic aids should be employed.

The importance of treating the mild as well as the more severe cases of acute nephritis is stressed. The fundamental principle in treatment is designed to secure as complete rest as possible for the inflamed kidney The patient should be put to bed and kept there until he has recovered from the disease or it has become chronic. If albumin, red blood cells and casts persist in the urine after 3 months and other evidence of inflammation, such as hypertension, reduced urea clearance, impaired concentration ability, or rapid sedimentation rate, is present, it may be assumed that chronic nephritis has developed and further rest in bed will be of no avail. Foci of infection should be removed, however, and it is desirable, if possible, to wait until the acute stage has passed The intake of protein and Calories may be disregarded during the first few days of the acute stage The amount of fluid advised varies according to the degree of renal insufficiency. If there is oliguria or anuria with a rising level of nonprotein nitrogen, sufficient fluids should be given by mouth or by vein to promote diuresis. If there are hypertension and edema of the brain with increased pressure of the cerebrospinal fluid or evidence of mild cardiac weakness, fluids must not be forced, for they may aggravate these complications. The presence of edema is not a serious matter and should not be the deciding factor for or against the administration of fluid. For the anemia, if present, large doses of *iron and ammonium citrate* may be given *Diets* should be rich in protective foods, particularly *vitamins*.

Nephrosis—The question of whether lipoid nephrosis is in itself a clinical entity or whether it is simply an atypical manifestation of chronic glomerulonephritis is far from being settled. In recent years the general trend has appeared to be that it is simply a form or a stage which occurs in certain instances of chronic glomerulonephritis. However, F. D. Murphy, L. M. Warfield, J. Grill and E R Annis98 believe that there is a primary form of lipoid nephrosis. They agree that this is rare and that in most instances the nephrotic syndrome is part of a chronic glomerulonephritis. They point out that an important factor in making this type of distinction is the length of time over which the patient is observed clinically. In their opinion, the chief distinguishing point is the ultimate outcome, the prognosis in pure lipoid nephrosis being favorable in contrast to

	TABLE 4		
GLOMERULAR	Nephritis	(A11	Cases)

Rochester		Stanford	
Number	Percentage	Number	Percentage
<i>77</i>	52 6	5 7	37
15	142	64	41.5
14	13 2	33	21.5
40	•	24	•
146		178	
•	Number . 77 . 15 . 14 . 40	Number Percentage . 77 52 6 . 15 14 2 . 14 13 2 . 40 .	Number Percentage Number . 77 52 6 57 . 15 14 2 64 . 14 13 2 33 . 40 . 24

(Snoke: Am. J. Dis. Child)

the poor one in chronic nephritis with the nephrotic element

In 9 cases which they believed to be pure lipoid nephrosis, 6 have recovered completely. 1 is under observation and 2 have died. The histologic examination of the kidneys of the 2 patients studied postmortem failed to show evidences of chronic glomerulonephritis Degenerative changes characteristically described as features of lipoid nephrosis were present. In 1 case the special staining methods of Bell were employed, and not even thickening of the basement membrane of the capillaries could be demonstrated They point out that the fundamental change in lipoid nephrosis is the hyperpermeability of the capillaries of the This functional disorder is glomeruli associated with profound albuminuria followed by generalized edema. Whether or not this functional derangement is followed by a structural alteration is a problem not vet determined

According to L E Farr and D. D. Van Slyke⁹⁹ there is a close relation between the presence of edema and the level of the plasma albumin in the blood of children with the nephrotic syndrome. It is stated that edema can be controlled satisfactorily in most instances by simple restriction of salt, together with an adequate diet, when the plasma albumin level is above 12 grams per 100 cc. This critical level for children is

markedly lower than the critical level of 2.5 grams reported for adults by Moore and Van Slyke. Thus in a small child the albumin content apparently must fall lower than in an adult before persistent nephrotic edema results. The age at which the difference becomes evident cannot be stated, since most of the patients in this series were between 4 and 7 years of age.

An apparent reduction in mortality from the peritoneal syndrome complicating nephrosis as well as beneficial results in the erysipelaslike cutaneous lesions associated with nephrosis has been observed by C A. Aldrich and H. H Boyle 100 The amount of serum administered varied from 40 to 100 cc. and was given intravenously whenever possible The authors ask the question why patients presumed to have a pneumococcic infection should respond favorably to convalescent serum from patients with a streptococcic infection They suggest 2 possible reasons. One is that convalescent serum has long been known to have nonspecific beneficial effects in patients with various diseases. The second possibility considered is that the intravenous injections of this amount of normal serum may influence the nephrotic element favorably and thus put the patient in better condition to fight the peritoneal or the cutaneous infection.

Pyelonephritis

An instance of arterial hypertension apparently caused by unilateral renal disease and relieved by nephrectomy is reported by J. D. Barney and H. I. Subv.¹⁰¹ The patient was a white girl. 10 years of age, who was said to have had pyelitis 3 years previously. The abnormal findings in the urine consisted of a slight trace of albumin and 10 to 20 white cells per high-power field. The blood pressure was 185/130. The excised kidney showed extensive parenchymal atrophy and dilatation of the pelvis. It was thought that the renal atrophy might have been the result of a "burnedout" pyelonephritis. The blood pressure 21 months after operation was 98/60.

Lower Urinary Tract Infection

Acute pyuria due to dysentery bacilli has been reported by H. F. Dietrich¹⁰² and by E Neter 103 These reports are unique since they are the first recorded cases of lower urinary tract infection resulting from infection with dysentery bacilli without an antecedent history of dysentery. There were no distinguishing clinical features from lower urinary tract infections due to other causes While recovery may be spontaneous, the infection responds promptly to the administration of ammonium mandelate. It is pointed out that dysentery infections of the urinary tract may be of importance from the standpoint of public health

Perinephric Abscess

The employment of the lateral pyelogram as a diagnostic aid in perinephric abscess is suggested by J G Menville ¹⁰⁴ In making the pyelogram, the patient lies on the affected side, perpendicular to the x-ray film. The accuracy of the lateral pyelogram is dependent on the patient's being entirely perpendicular to the film, for if the side of the patient

away from the film is tilted back, the kidney nearest the film will normally cast a shadow anterior to the vertebral column. Lateral pyelograms in 3 cases of perinephric abscess presented a uniform, anterior, arclike displacement of the kidney and ureter on the affected side. Postoperative lateral pyelograms in the

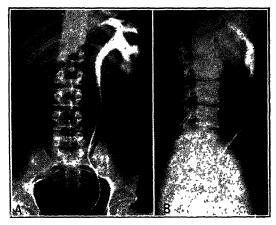


Fig 1 (Case 1)—A, a preoperative retrograde pyelogram of a patient with a pernephric abscess, showing the enlarged left kidney, with a slight blunting of the lower calices and a compression of the upper calix. The spine shows a curvature, with the concavity to the left side B, a lateral pyelogram presenting a marked anterior displacement of the kidney and an elongated, regular, smooth arclike displacement of the ureter (Menville I A M A)

same cases showed the kidneys and ureter to be in normal position with no evidence of anterior displacement. A lateral pvelogram in a very early case of perinephric abscess showed a minute anterior displacement of the kidney and ureter The author states that a similar displacement by other fluids is possible, he has seen such a condition following the extravasation of urine from a traumatic rupture of the kidney However. he states that in the absence of free fluid in the ruptured peritoneal space, he knows of no other condition that will produce a smooth, anterior arclike deformity of the kidney and ureter with the exception of an aneurism of the

PEDIATRICS

abdominal aorta. The characteristic deformities shown on the pyelogram of a patient with a perinephric abscess are illustrated in Fig. 1 and the postoperative return to normal is illustrated in Fig. 2.

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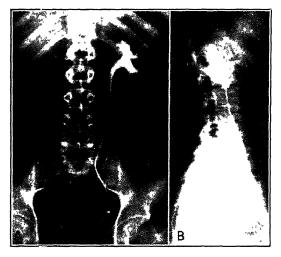


Fig 2 (Case 1)—A, a retrograde pyelogram made 4 months after operation, showing the pelvis and calices to have returned to their normal size and shape. The spine has also returned to a normal straight line (Compare with figure 1A) B, a lateral pyelogram made 4 months after operation, showing the kidney and ureter to be in normal position (Compare with figure 1B) (Menville J A M A)

Sarcoma of the Prostate

Sarcona of the prostate is not common According to P Katzen, H Cohen and M M Stemer¹⁰⁵ who report the occurrence of such a tumor in a boy 2½ years of age, there are reports of 152 authentic cases. While persons of any age may be affected, the highest incidence appears to be among the younger age groups. Approximately 25 per cent of the cases have occurred during the first decade of life and 11 cases have been reported in infants under 1 year of age.

The diagnosis of prostatic sarcoma has rarely been made before operation or autopsy. However, the authors point out that the diagnosis should not prove

difficult in children if the possibility of the lesion is borne in mind. Urinary frequency, dysuria or acute retention of urine, with or without accompanying difficulty in defecation are indications for prompt examination of the prostate by rectal palpation. A swelling of the prostate in a child is almost always due to sarcoma; the gland is usually smooth, regular and firm. Excretory urography is of distinct diagnostic value By means of the urogram there can be demonstrated elevation of the floor of the bladder due to the enlargement of the prostate and filling defects of the bladder if that organ is infiltrated by the tumor. There may also be demonstrated displacement or compression of the ureters and evidence of hydroureter and hydronephrosis. It is often difficult or impossible to perform cystoscopy because of obstruction of the posterior portion of the urethra Roentgenograms of the chest and of the bones may aid in establishing a diagnosis if metastases have occurred. Differential diagnosis should exclude the possibility of prostatic abscess, prostatic cyst and extensive retroperitoneal sarcoma involving the pelvis.

The prognosis is poor. To date there are no reported cures. Operative procedures should be limited to relief of symptoms. Drainage of the bladder is often necessary and is best accomplished by suprapubic cystostomy. Life may be prolonged by the judicious use of radium and roentgen therapy.

Vaginitis

A comparison of the efficiency of theelin, fever therapy, and sulfanilamide in the treatment of gonorrheal vaginitis has been made by C. M. Burpee, M. Robinow and J. T. Leslie. 106 The theelin was administered intramuscularly in oil; fever was produced by the intravenous injection of typhoid vaccine

and in 5 cases by the Kettering hypertherm; and the sulfanilamide was admintered orally.

Apparent cures following the intramuscular injection of theelin in oil as the only form of treatment were obtained in 41 of 47 cases. In 5 of these there were recurrences. Five patients treated with theelin and with 1 per cent silver nitrate jelly were cured and did not have recurrences.

Apparent cures following fever as the only method of treatment were obtained in 8 of 19 cases There was 1 recurrence. In 6 of 7 patients treated with fever during theelin therapy apparent cures could be attributed to the fever.

Apparent cures followed the oral administration of sulfanilamide as the only method of treatment in 11 of 22 cases One patient had a recurrence. Two patients were cured by a combined treatment with fever and sulfanilamide. One of these had a recurrence All cures due to sulfanilamide were obtained in less than 2 weeks Increase of the dose, prolongation of the treatment, and combination with fever therapy did not improve the results. The authors point out the need for further evaluation of treatment with fever and with sulfanilamide It is pointed out that there is still some uncertainty about the possible dangers of treatment with theelin These are stated to be (1) Development of secondary sexual characteristics, (2) a deleterious effect on the ovary, and (3) development of the upper genital tract. aiding the spread of the gonococcic infection to the tubes and ovaries An advantage of both fever and sulfanilamide is the shorter time required for treatment. The apparent cures from the use of theelin were obtained on the average between 20 and 50 days, whereas all cures with sulfanilamide were obtained in less than 2 weeks. The exact length

of time over which fever treatments were given is not stated. However, they do say that a "fair trial" consists of 2 or more fever treatments with resulting temperatures of 104° F. (40° C.) for at least 4 hours. It should, of course, be noted that in the authors' experience the percentage of cures with theelin was 87 per cent, whereas following the use of fever and sulfanilamide only 42 per cent and 50 per cent, respectively, were cured.

In estimating the dosages of the various estrogenic substances which are on the market, C Mazer and F. R. Schechter¹⁰⁷ advise that the rat unit be employed The dose of estrogen should be sufficient to cornify the vaginal epithelium and to reduce the pH of the vaginal secretions to a point below 6. They advise the continuation of treatment for 8 weeks, as a safeguard against the recurrence of the infection, even though there should be an earlier clinical and bacteriologic cure In their hands, hypodermic injections produced a clinical and bacteriologic cure in 78 of 81 children with a 10 per cent incidence of recurrence With vaginal suppositories of estrogen, they secured a clinical and bacteriologic cure in 33 of 34 children without any recurrence in 26 who were observed for a relatively long time All treatment was ineffective in 3 children who received as much as 1500 rat units daily for a period of 8 weeks. Such side effects as growth of pubic hair, uterine bleeding, and enlargement of the breasts were temporary and were more frequently encountered with hypodermic than with local treatment with estrogen.

The plan of | E Hoberg and L E Reck¹⁰⁸ for the treatment of gonorrheal vaginitis with sulfamilamide in ambulatory children is as follows.

1. First to Third Day—1 grain per lb. (142 mg per kg) per day.

- 2. Fourth to Seventh Day—½ grain per lb. (71 mg. per kg.) per day.
- (A) If the smear is positive at the end of the first week:
- 3. Eighth to Tenth Day—1 grain per lb. (142 mg. per kg.) per day
- 4. Eleventh to Fourteenth Day—½ grain per lb. (71 mg per kg.) per day.
- (B) If the smear is negative at the end of the first week:
- 5. Eighth to Fourteenth Day $-\frac{1}{2}$ grain per lb. (71 mg. per kg) per day.
- 6. Fourteenth to Twenty-eighth Day— ½ grain per lb. (71 mg. per kg.) per day.
- 7. If further medication is administered, the dosage is reduced to $\frac{1}{3}$ grain or $\frac{1}{4}$ grain per lb. (47 or 35 mg. per kg.) per day. In all instances, the drug is given in divided doses during the day. Bicarbonate of soda is administered with each dose of sulfanilamide

The authors report good results in 28 cases, questionable results in 9, and failure in 13.

Observations on the treatment of gonorrheal vaginitis with the Corbus-Ferry gonococcus filtrate are reported by L. E. Goldberg and K. Blanchard. 109 Twentyfour children with gonorrheal vaginitis received varied dosages of the filtrate ranging from $0.0083 \frac{1}{3}$ cc. initially, to 0.01 and 0.2 cc. at biweekly intervals over a period of 28 to 165 days. Of 18 patients cured by the Corbus-Ferry gonococcus filtrate, 5 had recurrences. Thirteen of the 24 patients in the series continued without trace of the disease. It is the author's impression that further experimental work must be carefully carried out before the value of the gonococcus filtrate as a cure for gonorrheal infection can be definitely determined.

GERMAN MEASLES

By Robert A. Lyon, M D

Viruses have been demonstrated in cases of German measles by H. Steinmaurer¹¹⁰ by means of fluorescent microscopy Specimens were obtained from the nose and throat secretions and from the blood of 20 patients with rubella and viruses were present in every instance In the blood, the virus occurred in a free state or was partially taken up by the leukocytes. During the acute stages of the infection when the virus was most plentiful, the other bacteria in the nose and throat secretions disappeared almost completely. The quantity of virus increased greatly on the first or second day before the appearance of the eruption, reached its peak on the day that the rash appeared and slowly diminished during the next 2 or 3 days.

Indication that German measles is a virus disease was also found in the ex-

periments of Y Hiro and S Tasaka ¹¹¹ The mucous secretions of the pharynx of 4 patients with German measles were diluted with physiologic saline solution and filtered to remove any bacteria. The filtrate was injected subcutaneously into 16 children who had not had the disease previously. A total of 8 patients developed typical forms of German measles and 2 had evidence of the infection but without the eruption. The incubation periods varied from 7 to 17 days.

Two instances of arthritis occurring during the course of German measles have been noted by T. Schultze ¹¹² The patients who were 21 and 25 years of age, contracted the illness during a mild epidemic of the disease. The arthritis developed about 72 hours after the onset of the illness and lasted for only a few days.

HEART DISEASE

By ROBERT A. LYON, M.D.

Arrhythmias

Repeated attacks of paroxysmal tachycardia in a girl of 8 years of age were relieved by the administration of mecholyl by F. H. Wright.¹¹³ The tachycardia was nodal in origin and in the early years of her life she had recovered from the attacks in 2 to 14 days without any treatment. When mecholyl was injected hypodermically in doses of $\frac{1}{12}$ to $\frac{1}{6}$ grain (5 to 10 mg.), the paroxysms were terminated rapidly. The treatment produces an asystole of the heart which must be observed carefully and if necessary can always be relieved by injections of atropine sulfate which restores the normal contractions. Only 52 reports of paroxysmal tachycardia in children have appeared in the medical literature between the years 1892 to 1935 Foci of irritation in the myocardium seem to disturb the normal cardiac cycle of contrac-The mecholyl checks the contractions of the heart, after which the normal mechanism of excitation may be resumed. In adults, a dosage of about ½ grain (30 mg) has been successful in interrupting the paroxysms and in restoring the normal rhythm

The subject of extrasystoles in children has been investigated by R A. Lyon and L W. Rauh ¹¹⁴ The irregularity was noted clinically in 45 per cent of the group of 782 children attending cardiac clinics, in 1 to 2 per cent of large groups of school children, and in 06 per cent of more than 5000 newly born infants. Extrasystoles were not only more frequent in older children, especially in those of school age, but the irregularity was about twice as frequent in those who had organic heart disease (4.3 per cent) as in groups of normal children (22 per

cent). Most of the extrasystoles were ventricular in origin and were not definitely related to pulse rate or to the position of the patient. In a group of 42 children with extrasystoles who were followed for a period of 1 month to 10 years, the extrasystoles were found to persist for more than 2 years in only 5 children. There was no evidence, however, that the irregularity caused any impairment of cardiac function or adversely influenced the child's rate of growth and development.

Chorea

Doubt has been expressed recently as to the importance of chorea in causing cardiac disease. In a review of 105 children with chorea, S. J. Usher¹¹⁵ found the incidence of cardiac involvement much less than in children with chorea and associated joint pains. A total number of 56 children had chorea as the only symptom of the rheumatic syndrome and 15 or 27 per cent of these developed heart disease. Seven of this group had had sore throats and respiratory symptoms which may have been responsible for the carditis. In 49 children, chorea and arthritis had both occurred, and heart disease developed in 32, or 65 per cent, of this group. In the author's experience no patient with chorea developed cardiac complications during periods of close observation unless there was a superimposed arthritic infection

Mental changes occurring in patients with chorea have been described recently by D. Shaskan. ¹¹⁶ Eight of his patients between the ages of 14 and 24 years had severe psychoses with symptoms of disturbed consciousness, emotional instability, hallucinations, increased or decreased

activity and some interference with normal thought processes. A second group of 9 patients between the ages of 8 and 21 years had mild mental disturbances characterized chiefly by emotional instability. A third group of 16 patients had no demonstrable mental changes except slight emotional instability. Fever therapy induced by injections of typhoid vaccine had little or no beneficial action on the severely affected group but seemed to aid the patients with milder mental symptoms.

Congenital Heart Disease

The mental development of 22 children with congenital heart disease has been studied by M. Ross 117 Various types of lesions were represented in this group but interventricular septal defects and patency of the ductus arteriosus were the most common In the entire group of 22 children, 2 had intelligence quotients below 50, and 7 had levels of 51 to 70 which placed them in the moronic Only 4 had intelligence levels within normal ranges. The average intelligence of these children with congenital heart disease was lower than that of 1000 clinic patients with other diseases Although the test group was too small to give results of statistical significance, the author was inclined to believe that congenital heart disease was another physical defect which might be searched for in studies which attempt to correlate mental deficiency with impaired health

In a review of coarctation of the aorta, G Eisenberg¹¹'s found that 15 reports of such lesions in children had appeared in the medical literature. He added the reports of 3 children, 2½, 3, and 9 years of age respectively, whom he had observed As a rule, no subjective symptoms were present and physical examination of the heart did not indicate any abnormality. The erosion of the ribs and the tortuous

vessels of the chest did not usually appear in early life and the electrocardiograms were generally normal. The most constant finding of diagnostic importance was the absence of pulsation in the femoral arteries. Other evidence of the disease in children was the higher blood pressure in the arms than in the legs and sometimes a coldness of the lower extremities. One of his patients, who was 5 years of age, complained of pain in the legs after walking short distances and discomfort beneath the ribs on the left side. A soft systolic murmur was noted at the cardiac apex and there were ventricular extrasystoles. The systolic blood pressure in the arms was 140 to 154 with no readings obtainable in the legs.

A case of double aortic arch has been described by I. J. Wolman¹¹⁹ and 6 other reports occurring in the literature were summarized Very few characteristic symptoms occurred during life which made the antemortem diagnosis possible, except stridor and cough with an aggravation of these symptoms during swallowing, due to the constriction of the esophagus by the large vessels Malnutrition and retraction of the head sometimes occurred It was thought possible that a diagnosis might be made with fluoroscopy, and that surgical treatment might be instituted to relieve the symptoms.

Ligation of a patent ductus arteriosus was accomplished successfully by R E Gross and J P Hubbard. The patient was a girl 7 years of age who had developed some cardiac hypertrophy and had a diastolic blood pressure of 38 mm of mercury as an average. After ligation of the ductus, the diastolic pressure rose to 80 Justification for such an operation was the removal of the extra load on the heart caused by the shunting of blood, and the possible prevention of subacute bacterial endocarditis which occurs fre-

quently as a complication of congenital malformations of the heart

Rheumatic Fever

Etiology—In a review of the climatic distribution of acute rheumatic fever, C. A. Mills¹²¹ has found that this disease, like the infections of the respiratory tract, is most frequent in the storm areas of the Temperate Zone The highest death rates from this disease in the United States have occurred along the north Atlantic seaboard, in the Great Lakes district, and the western mountain region These territories seem to be especially subject to storms and great fluctuations of temperature, humidity, and air pressure In contrast, the areas in which rheumatic fever is least common are some of the southern States and especially the southwestern States, such as New Mexico, Arizona, and Southern California, where temperatures are higher and storm changes least frequent author recommended migration to the southwestern States for periods of years as the best treatment of rheumatic fever ın children

The familial incidence of rheumatic fever has been investigated by R. L. Gauld, A. Ciocco and F. E. M. Read ¹²² Medical histories were obtained from the families of 96 children with rheumatic fever and 33 other children attending a tuberculosis clinic. Rheumatic fever was found to have occurred in 1 or both parents of 44.8 per cent of the group of children with that disease as compared with an incidence of 12.1 per cent in parents of the control series.

When the total number of children of the grandparents was classified in regard to the occurrence of the disease in their offspring, it was found that rheumatic fever occurred in much higher percentages when 1 or both parents had had the infection than when neither had been affected. The mothers who had rheumatic fever had about twice as many girls as boys with the disease, and maternal aunts and uncles had rheumatic fever much more frequently than those of the paternal side of the family. These family tendencies suggested some hereditary predisposition towards rheumatic fever, although the possibility of infection and exposure as etiologic factors could not be excluded.

The relationship between streptococcal infections and rises in specific antibodies has been demonstrated by A. F. Coburn and R. H. Pauli. 123 The antistreptolysin titer of the blood of rheumatic patients has been shown to rise with the occurrence of streptococcal sore throats for a period of about 3 weeks and then decline rapidly unless the rheumatic infection continued to be active. In a series of 16 rheumatic patients, other antibodies (anti M precipitins) developed in a manner similar to the antistreptolysin. In a series of patients with other forms of streptococcal infection than rheumatic fever, the specific antistreptococcal lysins occurred for about 3 weeks unless other complications developed, in which case the titers increased as long as the complication persisted but were slower in reaching the maximum. Similar responses could be produced experimentally in animals with streptococcal infections but not with other types of infections.

The occurrence of streptococcal antifibrinolysin in patients with acute rheumatic fever has been studied by C B Perry. 124 In a series of 44 patients who had 57 attacks of rheumatic fever, antifibrinolysins were detected in 45 instances but the clinical course of the patients of the 2 groups was not different in any respect. In a group of 6 patients with chorea, the antibodies were found in only 1 case. In a third group of 15 patients with chronic rheumatic heart.

disease who developed hemolytic streptococcal sore throats without any recurrences of their rheumatic infections, the antifibrinolysins were detected in only 2 instances. Five of this series had had some increase in their pulse rates.

In a fourth series of 10 children with carditis who had developed hemolytic streptococcal sore throats, followed by definite rheumatic relapses, 6 had antifibrinolysins and 4 had none. The exacerbations of the latter 4 patients were much milder than those of the 6 other patients. The author concluded that the presence of streptococcal antifibrinolysins could not be definitely related to the acute rheumatic process itself, since they occurred in about as many normal patients who had streptococcal infections as in those with acute rheumatic fever. There was no definite correlation between the duration or severity of attacks and the presence and persistence of the antifibrinolysins

Pathological Changes - Variations in the cholesterol content of the blood of rheumatic fever patients have been observed by F. M. Offenkrantz 125 Since the amount of cholesterol in the blood of normal patients varies considerably, it was difficult to determine any standard figures which could be considered as normal for an entire group. Of greater importance was the determination of the fluctuation of the cholesterol at different times in the same patient. During attacks of acute rheumatic fever, children had a diminution of cholesterol levels in the blood, most marked at the time of a severe attack or immediately preceding death. The total fall in values was mostly due to a decrease of the ester cholesterol fraction so that the relative percentage of free cholesterol was often elevated. In patients with chronic passive congestion in which the liver was involved, the flareup of a rheumatic infection usually

resulted in an increase in both the ester and the free cholesterol. High cholesterol levels which persisted in spite of disease were noted in a small group of overweight patients. This group was composed of good-natured extroverted types of individuals and the author was interested in speculating that certain psychogenic factors might influence cholesterol levels. In the majority of children, the tendency of the ester fraction to decrease in amount, leaving the free cholesterol relatively increased, was thought to have been a result of an increase of work on the part of the body This activity broke down certain tissue elements which were consumed or excreted; a mechanism of body defense against disease which may be controlled by the endocrine or the reticuloendothelial system

The course of the anemia of rheumatic fever has been studied by J. P. Hubbard and M H. McKee 126 A series of 17 patients between the ages of 5 and 16 vears who had exacerbations of rheumatic fever and severe forms of heart disease were studied over long periods of hospitalization. An anemia developed in every patient during the time of the acute manifestations of the rheumatic fever and improvement in the blood was noted during convalescence During the acute stages of infection, the color index was generally low but there were no characteristic changes in the size of the erythrocytes.

Measurements of the serum bilirubin did not show any definite variation from normal values during the active stage of infection, but the amounts of urobilinogen excreted in the urine were larger than normal. Whether this was the result of rapid blood cell destruction or of liver damage could not be determined. Reticulocyte counts indicated that the activity of the bone marrow was depressed during the acute stages of the

disease but many new erythrocytes were produced during the convalescence. Since the anemia developed so rapidly during the acute stages of exacerbation, there seemed to be a destruction of red blood cells as well as a depression of bone marrow activity. It was the conclusion of the authors that the presence of an anemia in a rheumatic fever patient might be another indication that the disease was still in an active stage.

Anemia in rheumatic infections has been found by G. Gezelius¹²⁷ to follow very closely the increase in sedimentation rate. In a series of 31 children, the anemia and the increased sedimentation rates were greatest in cases in which the rheumatic infection was most severe. In some instances the hemoglobin was reduced in greater proportion than the number of red cells but in severe infections both the hemoglobin and red cell counts were depressed. The administration of reduced iron did not seem to have any effect on raising the levels of hemoglobin or in decreasing the sedimentation Only when the infection subsided did both of these determinations return to normal The authors advocated routine hemoglobin determinations to corroborate the information obtained from sedimentation rates in regard to the status of rheumatic infections

Diagnosis—The relationship between growing pains and rheumatic fever in children and adolescents has been reviewed by J C. Hawksley ¹²⁸ In a group of 115 children having symptoms of growing pains, 85 per cent had muscle tenderness, usually in the calf of the leg, behind the knee, and less frequently in the back, shoulder, arm, and the instep of the foot. The joints themselves were not painful, swollen, or red. Very frequently the cause of such pain seemed to be flat feet, knock-knees, scoliosis or poor posture, and adequate orthopedic

treatment usually relieved the symptoms. A large number of such patients also had other vague complaints. Some had chronic catarrhal inflammation of the nose and throat, others had vasomotor disturbances, or were emotionally unstable. The blood counts, sedimentation rates, and electrocardiograms of such children were usually normal.

Frequent observation of these children did not reveal any illness such as sore throat or respiratory infection preceding the occurrence of the growing pains, and heart disease rarely developed. specific growing pains occurred in about one-third of a group of 505 children between the ages of 4 and 14 years, in a London institution, and more frequently in some other groups in other localities It was the conclusion of the author that growing pains, as defined above, comprise a clinical entity and must be differentiated from the joint manifestations of true rheumatic fever. There was no evidence that any relationship existed between the 2 conditions.

A differentiation between growing pains and true rheumatic fever has been made by M J Shapiro.¹²⁹ Such a distinction was of prognostic value, since carditis rarely developed in children who have growing pains only Of a series of 100 children with rheumatic heart disease, 84 per cent had histories of acute polyarthritis, chorea, or both, and the remaining 16 per cent had no history of either symptom. On further questioning of the parents of 16 children, a history of subacute rheumatic joint pains was obtained in 10 instances

Children with atypical pains, or growing pains were usually well nourished; localized the pain in the muscles of the lower extremities as a rule; complained mostly at night, and were free from symptoms in the morning; and found relief in treatment with warm applica-

tions or massage. These pains did not occur more frequently in winter than in summer and were not accompanied by epistaxis, skin rashes, fever, elevations in leukocyte counts or sedimentation rates, as in the case of true rheumatic arthritis.

Graphic records of the heart sounds of 105 normal children of various ages from 5 to 17 have been studied by M. H. McKee.¹³⁰ A splitting of the first or second heart sound occurred in 63 per cent of the cases. The split first sounds were noted most frequently at the apex and the split second sounds were clearest at the pulmonic area. Third heart sounds were audible with a stethoscope in only 6 cases but the graphic sound records indicated that they were present in 66 per cent of the series, usually 011 to 015 seconds after the beginning of the second sound In 94 per cent of the group, a slight vibration occurred shortly before the first sound and this was interpreted to be auricular in origin. In the auscultation of the heart of this group of children, apical murmurs of little siginficance were noted in 5 of the 105 children The graphic sound records, however, produced evidence of apical systolic sounds in 90 per cent of the entire group No diastolic murmurs were noted. It was the conclusion of the author that the splitting of the first and second heart sounds and the presence of a third heart sound had no pathological significance, and that very soft murmurs which can barely be heard at the apex probably have no significance

Sound records of children with rheumatic fever were then compared with the records of normal children by M. H. McKee ¹³¹ The children with possible or potential heart disease who had had attacks of rheumatic fever but had no evidence of cardiac disease showed the same type of sound records as did the

normal children. No diastolic murmurs occurred in this series. In 35 children with mitral insufficiency with a readily audible murmur at the apex which was blowing in quality, the sound tracings were very similar to the normal group except that the murmurs were higher in pitch and there was a tendency for the accentuation of the second sound. Thirteen of this group had audible diastolic murmurs with the stethoscope but the graphic records showed that 30 children had diastolic murmurs following the third heart sound The patients with mitral insufficiency and stenosis frequently had greatly accentuated second heart sounds at the pulmonic area and the systolic murmurs were generally much greater in intensity than did the normal children The sound tracings of the diastolic murmurs varied considerably, but some of them were more intense than either the first or the second sounds and lasted throughout diastole The characteristic murmur was a sound noted at the beginning of the third heart sound and continuing for a variable period of time throughout diastole There was always a soundless interval between the second and third sounds. The graphic records of the sounds of the hearts of children with active carditis occasionally showed a decrease or an absence of sinus arrhythmia, an increase in the length and intensity of murmurs, and occasionally the appearance of new murmurs amplitude of the first sounds occasionally decreased and diastolic murmurs displaced the third heart sound. It was concluded by the authors that the frequent sound record of patients with heart disease would indicate somewhat the progress of the heart condition, especially with respect to the length and intensity of the diastolic murmurs

Skin Lesions — Two patients with erythema annularc associated with acute

rheumatic fever have been described by H. Abramson and A. M. Tunick. 132 In 1 patient, the lesion occurred at the onset of the disease and persisted for 2 weeks; in the second patient, the dermatitis developed before the onset of the joint pains and lasted for a week. In these 2 instances the duration and persistence of the erythema annulare seemed to be a manifestation of a severe rheumatic infection although it is generally stated that such skin manifestations are unrelated to the severity of the rheumatic disease The authors believed that this type of skin lesion occurred with other types of infection than rheumatic fever and therefore it must not always be considered as a specific manifestation of that disease.

Treatment-The effect of the removal of tonsils and adenoids in patients with rheumatic fever has been reviewed by W. B Allan and J W. Baylor¹³³ in a series of 108 patients followed for a period of 1 to 23 years. Recurrences of rheumatic infections occurred in 43 5 per cent of patients and carditis in 47 1 per cent, which were lower rates than occurred in the community as a whole Among 47 patients who had had rheumatic attacks but no cardiac lesions before tonsillectomy, only 6 developed heart disease in later years after the operation and it was concluded that the evidence in favor of removal of tonsils and adenoids in rheumatic patients was sufficiently great to recomend the procedure

Operations such as the removal of tonsils and adenoids are a greater risk in children with active rheumatic infections than in normal patients. H L. Bacal and R. R Struthers¹³⁴ have observed the effect of such operations on the sedimentation rates of 100 children with rheumatic fever of various forms and stages. Comparisons were made with the

results in 50 other normal children. As a rule, operation upon rheumatic patients caused more frequent rises in sedimentation rates, greater losses of weight, more frequent postoperative hemorrhages, and more protracted periods of recovery than upon normal children. Occasionally, the slight elevation of sedimentation rates of children who had no other manifestation of activity of rheumatic disease over a long period of time, dropped rapidly to normal after the operation. This beneficial reaction probably resulted from the removal of tonsils which had been foci of infection.

Some of the methods of treatment of rheumatic heart disease have been reviewed by H. B. Taussig. 135 She advocated the use of salicylates in doses of 1 grain per pound (140 mg. per kg.) of body weight. When the dosage per 24 hours is greater than 30 grains (2 Gm.), alkali, such as sodium bicarbonate or potassium citrate, should be added in equal amounts to counteract the symptoms of acidosis. Magnesium carbonate has been found to be of value in enhancing the beneficial effects of the salicylate treatment For abdominal pain associated with rheumatic fever, pyramidon may be found to be effective. Rest in bed is always the most important form of treatment during the active stages of rheumatic fever. The activity of the infection must be determined by the temperature of the patient and by laboratory tests, especially the sedimentation rate. Regardless of the time required for the rheumatic infection to subside the child should be kept in bed throughout this period of time

Cardiac failure rarely occurs as the result of chronic heart damage, but is due to the active rheumatic process Hearts which have been damaged previously and show evidence of enlargement are less apt to withstand subse-

quent infection but it is the infection itself which causes the final failure of the circulatory system. *Digitalis* is valuable during the chronic stages of rheumatic heart disease and especially when there is cardiac enlargement, chronic congestive failure or auricular fibrillation over long periods of time, but during the acute stages of rheumatic fever it is questionable whether digitalis has any beneficial effect.

A search for some substance in the blood of rheumatic fever patients which might activate or combat the disease has been made by M. Friedman, R. Klein and P Rosenblum 136 Blood samples withdrawn from patients during the acute phases of their rheumatic attacks were passed through Berkefeld filters and injected back into the same patients Slight exacerbations of the disease seemed to occur 3 to 11 days after the injection When the serum was administered to other patients who were convalescing from the infection no results were obtained The blood of convalescent rheumatic patients was then administered to 4 individuals who were suffering from acute attacks of the illness and no beneficial reactions occurred Although 30 to 140 cc of convalescent serum were injected intravenously, no evidence of clinical improvement in this group of 4 individuals could be detected

Quinidine has been administered to 12 children with heart disease, in doses approximately the same as for adults, by C R Messeloff ¹³⁷ Ten children between the ages of 8 and 14 years with rheumatic heart disease received 9 grains (0.58 Gm.) daily as an initial dose and then increasing amounts up to 45 grains (3 Gm.) a day. There were no systemic symptoms of a toxic nature. The earliest electrocardiographic changes consisted of a decrease in the amplitude of the T waves in all leads. When the dosage had

mounted to 30 grains (2 Gm.) a day, there were occasionally some increase in width of the QRS waves and a prolongation of the A-V conduction time. In 1 child with auricular premature contractions, 30 grains (2 Gm.) daily of the drug succeeded in abolishing the irregularity. In another child with a bundle branch block, probably the result of a congenital defect of the interventricular septum, quinidine, in doses of 20 to 30 grains (1.3 to 2 Gm.) daily, prolonged the ORS interval but did not affect the PR interval or T waves. The author concluded that quinidine might be employed in children as in adults without harmful results

Sulfanilamide has been used to prevent recurrent attacks of rheumatic fever by C B Thomas and R France. 138 A group of 30 individuals, between the ages of 14 and 36 years, received 15 to 20 grains (1 to 13 Gm) of the drug each day in 3 divided doses other patients who were observed during the same period of 7 months, served as a control group. Those who received sulfamilamide were free from major attacks of the disease throughout the entire period of time, and only 2 had minor attacks, while 4 of the control group had major attacks, and 2 had minor attacks of rheumatic fever. Beta hemolytic streptococci were absent from the throats of the treated patients and 4 of the control series had such streptococcic infections during the period of observation

Sulfanilamide seemed to have some prophylactic value in the prevention of rheumatic attacks in a group of children treated by A. F. Coburn and L. V. Moore 139. When the drug was administered to a series of rheumatic patients who had developed sore throats, the occurrence of exacerbations of the rheumatic fever was not prevented, but when the sulfanilamide was given to such pa-

tients before the development of streptococcal reinfections, the number of exacerbations seemed to be greatly reduced as compared with a control series. Thirty grains (2 Gm.) of the drug were administered daily through the winter months without any reactions or ill effects from the therapy. All but 1 of a series of 80 rheumatic patients lived through a winter season without any streptococcal infections or exacerbations of their rheumatic fever.

Systolic Murmurs

Observations of apical systolic murmurs of 33 children over a period of 10 years or more have been made by L. G. Steuer and M. H. Fineberg. 140 During this period of time 7 had developed mitral stenosis, 1 an aortic insufficiency and 1 a combined mitral and aortic lesion. This total of 9 patients constituted 27 per cent of the group who were followed. Twenty of the 33 patients, or 61 per cent, still had systolic murmurs at the apex and nothing more The remaining 4 patients, or 12 per cent, had lost their murmurs These figures corresponded entirely. very closely to those noted in a group of 100 patients who had been followed for 6 years or more, the results of which had been reported previously. Mitral stenosis usually developed within 1 to 9 years after the discovery of the original There was some indication murmur that high blood pressures developed more frequently and at earlier ages in children who had apical systolic murmurs than in normal children, but the number of the author's observations was too small to prove the point.

The subsequent course of systolic murmurs of 102 children has been followed by M. J. Shapiro. 141 The children varied in age from 5 to 15 years when first examined and they were observed for periods of 2 to 12 years. During this time 76 of the group retained systolic murmurs without any change in their characteristics. In 17 children the murmur had disappeared. In the remaining 9 children the diagnosis of congenital heart disease was made in 3 instances, rheumatic heart disease with aortic insufficiency in 1, and possible early hypertension in 5. Among the children who developed organic disease or possible hypertension, the intensity of the systolic murmur had increased and was transmitted towards the axilla and the back. The intensity of the murmur and the area of audibility were valuable aids in deciding whether or not organic heart disease was present. On the contrary the soft systolic murmur which was located close to the apex and did not replace the first sound seemed to be of less consequence and probably did not represent organic disease. Roentgenograms and fluoroscopic examinations of these patients were of considerable aid in detecting enlargement of the heart suggestive of the presence of organic lesions, but electrocardiograms were of little value in making an accurate diagnosis of the borderline cases.

INFANT FEEDING

By Waldo E. Nelson

Metabolic studies in infants by S Z. Levine, M. A. Wheatley, T. H Mc-Eachern, H. H Gordon and E Marples¹⁴² indicate that the customary diet

employed in infant feeding, containing approximately 120 Calories, from 4 to 5 Gm. of protein and 160 Gm. of fluid per kilogram of body weight are ade-

quate to ensure the deposition within the body of organic materials and water which qualitatively approximate the chemical composition of infantile tissue and which quantitatively fulfill the requirements for satisfactory growth

Breast Milk

A method for the administration of complementary feeding to a nursing infant without removing him from the breast has been described by A. E. Russell and T. McKeown. The method is designed to supplement breast feeding during the periods of temporary failure or inadequacy of lactation without removing the sucking stimulus. The authors cite several instances in which by this method they have been successful in reinstating lactation.

Their method is as follows A number 2 or 3 rubber catheter is attached to a glass tube which passes through a rubber stopper at the teat end of an ordinary 4 oz. boat-shaped feeding bottle which is encased in a flannel cover and pinned to the mother's dress at shoulder level. The infant is weighed and put to the breast and allowed to suck until the breast is empty or as long as he will do so peacefully. As soon as there is evidence of refusal, which may be immediately if the breast is empty, the catheter is pushed gently into his mouth, care being taken to make sure that it passes between his gums with the nipple. The infant does not appear to be aware of the catheter and sucks vigorously as soon as milk flows into his mouth. The rate of flow is controlled by the valve at the top of the bottle and by pressure of the mother's finger on the catheter. Finally the breast should be emptied by manual expression and the expressed milk set aside for the next complementary feeding.

Evaporated Milk

In view of an impression that babies fed irradiated evaporated milk were more likely to develop diarrhea than were infants fed nonirradiated milk, C. G. Grulee, H. N. Sanford and M. Lewison¹⁴⁴ have made a comparative study of the effect of these 2 foods on 2 different groups of infants over a period of 2 years. The group fed the nonirradiated evaporated milk was given viosterol as an antirachitic agent.

The average number of stools was practically the same for each group (2.0 per day for the irradiated milk group and 23 per day for the nonirradiated milk). In certain of the babies in both groups, there was a tendency occasionally to have more than 3 stools per day. This tendency occurred oftener in younger infants. It was slightly more marked during the first week in the non-irradiated milk group and during the later months in the irradiated milk group.

The average gain per month was the same in both groups (1.3 lb. per month). None of the infants in the group given irradiated evaporated milk showed any signs of rickets either clinically or roent-genographically. Four infants in the group given nonirradiated evaporated milk and viosterol showed slight signs of clinical rickets, but of these only one showed signs of rickets by roentgenogram

Soft Curd Milk

Laboratory tests by F. J. Reithel and I A. Manville¹⁴⁵ indicate that the addition of dehydrated apple to milk results in a lowering of the pH and the production of a soft curd. When dehydrated apple was added to a cow's milk formula, the initial pH of the formula was reduced from 6.5 to 5.7. Reduction in the buffer value of this cow's milk-apple

formula by the addition of lactic acid was less effective than it was in a cow's milk formula without the addition of apple powder. With hydrochloric acid, however, the addition of apple distinctly lowered the pH throughout the entire range studied. In other words, when apple was added to the milk formula, not only was the initial pH lower, but less hydrochloric acid was needed to bring the pH down to a given point. The authors advise the addition of dehydrated apple to milk formula up to 4 to 5 per cent in infant feeding when cow's milk is digested with difficulty.

Banana

J. D. Craig¹⁴⁶ has fed ripe banana as the first solid food for infants 6 weeks of age and older as a routine practice in the New York Foundling Hospital during the last 7 years. He believes that the banana's digestibility makes it an ideal first food to offer infants to accustom them to solid foods. When given with cod liver oil, it increases the ease of administering the oil to small infants. He also recommends mashed, ripe banana as the first solid food for infants who are recovering from diarrheal disorders.

Transmission of Drugs in Breast Milk

Barbiturates—Further studies on the transmission of drugs through breast milk are reported by R. M. Tyson, E. A Shrader and H. H. Perlman. 147 Barbiturates when administered to a lactating mother are transmitted by breast milk, as shown by chemical analysis. Analyses of individual specimens of milk after administration of barbiturates in ½ grain (30 mg) doses at stated intervals, although amounting in the aggregate to 2 grains (130 mg) per day, do

not show as high a percentage of positive reactions as do similar specimens after the administration of 1½ grains (94 mg.) at bedtime. Thus, concentrated doses seem to have more effect on transmission than do accumulative ones. In only 2 of the 41 cases was there any clinical evidence of effect of the barbiturates in the infant.

Bromides—Their data, both chemical and clinical, also indicate that sodium bromide is transmitted through breast milk in sufficient quantities to produce an effect upon the nursling. In 37 of 38 specimens of milk analyzed there were positive tests for bromides. Clinical evidence of transmission was manifested in the infant to a marked extent in 4 cases, although in every case there was a marked diminution in the irritability of the child as well as of the mother. The amount of sodium bromide administered to the mother was equivalent to 15 grains (1 Gm.) every 4 hours

Sulfanilamide—According to the observations of H. L Stewart, Jr., and I P. Pratt, 148 free sulfanilamide is excreted in human breast milk in concentrations closely corresponding to the values present in the blood stream. When oral administration of sulfanilamide is discontinued, the concentration in the milk falls rapidly. Babies fed entirely on breast milk did not show clinical evidence of toxic manifestations when sulfanilamide was present in the breast milk in concentrations of 1/10 grain per $3\frac{1}{3}$ oz (7 mg per 100 cc) Traces of the drug were present in the blood of the baby. The urine of these babies contained amounts varying from $\frac{1}{60}$ to $\frac{1}{25}$ grain per $3\frac{1}{3}$ oz (1 to 26) mg per 100 cc.) during a 24-hour period It is stated that a nursing baby cannot obtain an adequate therapeutic dose through the milk of a mother

receiving an average clinical dose. Sulfanilamide was also present in the cord blood and amniotic fluid of 6 women

following the oral administration of 5 grains (0.3 Gm.) of the drug every 4 hours throughout labor.

JUVENILE DELINQUENCY

By Robert A. Lyon, M.D.

A survey of the behavior of delinquent girls who had been discharged or paroled from an Iowa State Institution was conducted by M. Skodak.149 The majority of these girls had been committed to institutional care because of some sexual delinquency. Their ages varied from 10 to 18 years with a median age of 16 years at the time of entering the institution and 69 per cent had lived previously in cities with populations of 8000 or more. Only 15 per cent came from villages or rural communities of less than 2000 inhabitants The social-economic levels and intelligence quotients were below averages of the general population, and at least 69 per cent had come from broken homes.

A total number of 103 girls was selected as a sample for study and two-thirds or more of this group had been returned to the institution after the first parole About 39 per cent of the group were discharged because of marriage while on parole and 37 per cent were discharged because they had reached the legal age of maturity. The girls who married tended to be of lower average intelligence, had as a rule been committed to the institution at earlier ages; and had therefore spent more time there than the other girls.

Of the entire group of 103 girls, 68 per cent were found to have made satisfactory adjustments in society, 20 per cent had adjusted poorly and the remainder could not be followed. The factors which seemed to be correlated

with success after leaving the institution were the early age of admission and discharge, and the smallest amount of previous institutional experience. Girls with lower levels of intelligence did better as a group than those of higher levels. The patients who had made the poorest records after leaving the institution frequently had had broken homes which had necessitated the institutionalization of other members of the family.

It was concluded by the author that such results as the above can only indicate general trends and that the application of treatment to any delinquent girl requires individual care and study.

A report of the recent trends in the treatment of juvenile delinquency in Germany has been made by O. Kirchheimer. 150 There seems to have been a recent increase in crime among young The figures from a typical juveniles city (Hamburg), indicated that the incidence had more than doubled in children of ages of 14 and 15 years, in the year 1936 as compared with the year 1931 There was a slight decrease in the number of children 17 years of age. Increases occurred especially in such crimes as larceny and sex offenses which were thought to have been influenced by poor housing conditions, and crowding in labor projects and camps. Emphasis in treatment has been of a disciplinary nature and even the physical activities of the children have been strictly supervised MEASLES 571

with a decrease in the amount of time allotted to voluntary sports and recreation. Handicrafts of an educational nature have been sacrificed to the teaching

of traditional prison trades. In the new bureaucratic type of government, little attention has been given to new methods of treatment of the juvenile offenders.

MEASLES

By Robert A. Lyon, M.D.

Complications—A fatal case of morbilli bullosi in a 17-year-old girl was observed by E. James and A. A. Miller. ¹⁵¹ This was the first instance of such a complication of measles occurring in a series of more than 2500 patients with the disease.

A series of 14 children with encephalitis following measles has been reported by M. G. Peterman and M. J. Fox. 152 A previous report of 13 patients of an earlier epidemic of measles had been made by the authors and the symptoms and characteristics of the total number of 27 patients have been summarized All but 1 of the children were less than 10 vears of age and the symptoms of encephalitis which usually appeared about 4 days after the appearance of the rash. consisted of drowsiness or coma and convulsions. The pupils were generally dilated, the reflexes exaggerated, the extremities spastic and the neck stiff The temperature at this stage was about 102° F (39° C) as an average and a polymorphonuclear leukocytosis was generally present The cell count of the cerebrospinal fluid was elevated above normal and the cells were predominantly lymphocytes The colloidal gold curve showed a response in the middle meningitic zone (such as 0123321000) mortality rate of the entire group of 27 patients was 296 per cent and residual symptoms occasionally persisted in those who survived Treatment of the condition was entirely symptomatic For the relief of cerebral edema, magnesium sulfate was given by mouth or intramuscularly. Convalescent serum seemed to be of no value in this stage of the infection and the authors warned against excessive treatment with fluids, serums and blood transfusions, which might overload the circulatory system.

Tolerance tests for vitamin C during the course of measles were made in 15 patients by P Robert. ¹⁵³ In 12 instances, a vitamin deficit of varying intensity was noted.

Treatment-Sulfanilamide was employed in the treatment of 400 measles patients by A. R. Thompson and C. R. M. Greenfield 154 The dosage varied from $7\frac{1}{2}$ grains (0.5 Gm.) daily for infants less than a year of age to 30 grains (2.0 Gm) daily for children 10 to 15 years of age, and the treatment was continued for 10 to 12 days Some patients with severe forms of the disease received larger doses for longer periods of time. The drug was administered orally in a sweetened drink and no complications other than cvanosis were noted. A series of 819 patients served as a control group but there was a tendency to give the specific therapy to the children who were most severely ill

Complications occurred much less frequently in the treated group of children and incidence of otitis media fell from 118 per cent in the control series to about 29 per cent in the treated. Pneumonia developed in 48 per cent of the

control patients and in only 1.7 per cent of the treated series. The drug seemed to have very little effect in reducing the fever of the infection and it was concluded that the virus of measles was not affected by the sulfanilamide but that the most beneficial results were the prevention of complications. In general, the epidemic of measles which served for this study was mild and the authors believed that further trials with the therapy should be made before definite conclusions were reached in regard to its value.

Sulfapyridine was administered to 38 patients with pneumococci types of postmeasles pneumonia by H L. Hodes, W C. Stifler, E Walker, M. McCarty and R G. Shirley. 155 Favorable results were obtained. The fever disappeared rapidly and definite improvement occurred in every instance within 48 hours after the sulfapyridine was given No complications from the therapy were noted.

Proseptasine, a compound related to sulfanilamide, was employed with success in the treatment of measles patients by J. C. Hogarth 156 He administered the drug to 158 measles patients for a period of 10 days. A series of 171 patients of similar age, with measles of approximately the same severity, served as a control group. Although the epidemic as a whole was mild there was only about one-half as much pneumonia and one-third as much otitis media in the treated group as in the control group Enteritis did not respond to the therapy but occurred as frequently in one as in the other series. The drug was well tolerated and seemed to be especially valuable in the prevention of complications of measles which are apt to be due to secondary invasions of the streptococci.

Convalescent serum administered during the few days previous to the outbreak of the rash of measles has been

advocated by J. L. Kohn, I. F. Klein. and H. Schwarz. 157 A group of 12 children received 50 cc. or more of the convalescent serum intravenously, 1 or 2 days before the rash developed, and 10 of these had modified attacks of the disease. In 6 other children, 40 to 45 cc. were given intravenously and 5 of this group were definitely benefited by the injections. Smaller doses had less influence on the course of the disease. In order to determine whether or not the disease might be modified by the injection of serum later in the course of the infection, additional doses were given to 4 patients and this procedure likewise seemed to have a beneficial action in reducing the severity of the infection.

Of a total number of 24 children treated, 4 had very severe infections due to such complications as peritonitis, pneumonia, rheumatic fever, and croup The authors felt that the serum was definitely responsible for the recovery of these children

The injection of a serum concentrated to one-third of its original volume produced a favorable response in only 1 of a group of 4 children. It was the conclusion of the authors that 40 to 50 cc of convalescent serum injected intravenously, at least 1 day before the appearance of the eruption, gave favorable results in modifying the course of the infection If adults were used as the source of the blood, 125 cc of whole blood would probably be needed Either form of therapy would be especially important for children who are malnourished or suffering from other infections at the time when measles was contracted

Injections of *immune adult serum* early in the incubation period of measles had beneficial effects in the group of children observed by L. R. Lempriere ¹⁵⁸ The serum was administered to 96 boys in doses of 20 cc. on the fifth to seventh

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day after exposure. A group of 28 boys who were not treated, served as a control group. The disease was much milder in the treated patients and the number with complications was smaller (4 per cent) than in the control group (18 per cent). It was thought probable that larger doses of serum should be employed in older children.

Satisfactory results from the use of placental extracts in modifying an epidemic of measles were obtained by T. N. Parish. 159 Such an epidemic started in a school of girls whose ages ranged from 13 to 17 years. Injections of 4 cc. of immune globulin were given to 47 patients shortly after their exposure to the infection. Pain at the site of injection occurred in a good many instances and 1 girl had a temporary elevation of temperature but in no case could the reactions be called severe. With this dosage the infection was not prevented in any of the injected patients but the disease tended to be mild in nature. Only 1 patient developed a complication, consisting of an otitis media which required drainage. It was believed that a larger amount of placental extract might have protected some of the children from the infection but in such an age group, a modification of the disease with the development of permanent immunity was the desired result

The management of an epidemic of measles in an institution has been outlined by F. G. Hobson ¹⁶⁰ In his opinion the healthy children should be allowed to contract the disease, providing no other infections were current within the institution Children who are below normal standards in health and nutrition should be adequately treated with convalescent serum, immune adult serum or immune globulin to attenuate the attacks of the infection. In this manner the maximum amount of immunity should be

provided, the number of complications should be small and the epidemic should be mild. Such a program was followed in a school of 95 boys of which 56 had not had the disease previously. All of the delicate susceptible children were given 10 cc. of convalescent serum on the sixth day after exposure to the infection. The remaining group of children who were in good health and had not had recent respiratory infections were allowed to contract the disease in a normal manner. No complications occurred during the course of this epidemic The children who received the serum had attenuated attacks of the disease Under ordinary situations this plan should prove to be very satisfactory but under certain conditions in which the size of the school or the type of patients attending the institution may introduce variable factors, it might be necessary to change the routine and to provide the children with more adequate protection against the infection

In the evaluation of the effectiveness of protective measures against measles, care must be taken to determine the source of exposure of the group of children under consideration. S Karelitz¹⁶¹ has summarized the results of immunization of children against measles by the use of convalescent serum, immune adult serum, and a globulin extract of serum

In a series of 314 cases the number of failures to protect or modify measles seemed to depend upon the amount of exposure. The number of failures of treatment of children who had been exposed in homes of poor hygienic levels was as high as 23 per cent, while the number of failures in children who had been exposed more casually in other situations was only 7 per cent. As a rule, the dosage of protecting agents is calculated upon the age and size of the child and the potency of the preparations,

but in some instances, the intimacy of contact and possibly the resulting quantitative increase of initial infection may demand larger doses of serum in order to secure the desired result. Therefore, the children from homes of poor hygiene and crowded living conditions may have severe exposures to measles and require larger amounts of the serum for protec-

tion or modification of the disease than children exposed in homes of good hygiene or in hospitals, nurseries or playgrounds where contact is more casual. In the evaluation of the clinical results obtained from serum treatment of this sort, this factor of the quantity of initial exposure and infection must be borne in mind

MENTAL DEFICIENCY

By Robert A. Lyon, M.D.

The incidence of feeblemindedness in a series of 146 individuals with cerebral pulsy was investigated by J. T. McIntire 162 Only patients with motor handicaps were included in the study. The families of these patients seemed comparable in mental status, education and occupations to the rest of the population of that locality. The chief causes of the cerebral palsy seemed to be birth injury (63 per cent), intracramal congenital defects (19 per cent) and encephalitis (4 per cent) The examination of intelligence levels of these patients indicated that 18 per cent were definitely feeblenunded and 8 per cent were borderline cases. It seemed probable that the injury causing the motor paralysis was responsible for the mental retardation

The possibility of illness or accidents causing mental deterioration has been emphasized by B. Crothers. 163 In a series of 10 patients, he had observed, 1 had evidence of birth injury but the other 9 children had been well and apparently normal in mental development and behavior until some specific experience with disease or trauma. These illnesses and accidents included whooping cough, encephalitis, smothering by a cat, encephalopathy following an appendectomy, upper respiratory infection, lead

poisoning, alcohol ingestion, trauma and suffocation from smoke. Symptoms of convulsions, hemiparesis, and paralyses developed in several of these patients in addition to the mental deterioration. Encephalograms assisted in the detection of gross lesions of the brain

Mongolian Idiocy

In a study of some of the predisposing factors of mongolism, C R. Myers¹⁶⁴ reviewed the histories of 215 mongolian idiots in various institutions in Canada Comparisons between this group and a series of mental defectives who were not mongols, in regard to the occupational status of the father, the age of the mother at the time of the birth of their infants, the birth intervals, and the health of the mother, revealed no outstanding differences except the very high incidence of thyroid disease and acute nervous excitement in the mothers of the mongolian group Mongolism occurred most frequently in areas in which there was a high incidence of thyroid disorders. The dysfunction of the thyroid gland may also account in part for the lack of fertility of the mother and the subsequent retardation of growth and development of the infant, which are characteristics of mongolism It was not the author's

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conclusion that thyroid disease was the cause of mongolism but he thought it might be possible that some such glandular disturbance was one of several complex disorders which combined to cause this type of mental retardation.

A study of the structural changes which are common in all mongolian idiots has been made by C. E. Benda¹⁶⁵ in a series of 120 such idiots of various ages. In a summary of these findings the author emphasized the fact that these children grow slowly during the first 5 years of life and that increases in height usually cease after 15 years. The mongolian idiots are frequently underweight during the first 2 years of life but after the fifth year, and especially at the time of puberty, they may become overweight and even obese. At birth the skull is not smaller than normal but growth is very slow during the first 6 months of life, especially of the base of the skull so that the normal elongation of the head does not take place. The fibrous portions of the skull likewise grow at slow or normal rates so that the total size of the head is below average, as a rule The ossification of the long bones proceeds at an irregular rate and early ossification and fusion of the epiphyseal lines is often noted. From these measurements and observations the author concluded that mongolian idiocy is not the result of a racial mutation but is a disease beginning at some time during fetal life

Characteristic changes in the structure of the thyroid glands of 14 mongolian idiots between the ages of 9 days and 2 years have been described by C. E. Benda. The glands were generally smaller than average and yet showed evidence of hyperactivity with the acini distended with colloid, the epithelium low but overgrown in piles and convolutions. It seemed possible that some thyroid disturbance of the mother or a related dysfunction of some other endocrine gland might be the cause of these thyroid changes in mongolian idiots.

Treatment—The growth of 8 mongolian idiots treated with extracts of the thyroid and anterior pituitary glands over a period of 4 years has been followed by A. A. Werner, J. Lewald, G. A. Johns and D. Kelling. 167 These children increased in weight and height at approximately the same rates as did normal children Five other mongolian idiots who were not treated in this manner also grew at the same rate so that no definite influence on the physical growth of mongolian idiots could be attributed to these endocrine glands. Although the mongolian idiots tended to grow at normal rates, their stature was always somewhat below the averages of normal children Some of the children treated with the glandular extracts showed some improvement in their mental capacity but none of them developed beyond the ranges of idiocy.

MUMPS

By ROBERT A. LYON, M.D.

Complications — Meningoencephalitis has occurred with considerable frequency in the patients with mumps observed by H. Finkelstein. 168 In a series of about 40 such patients, lumbar punctures were performed soon after their admission to the hospital Of this group, 16 had abnormal cerebrospinal fluids and

these patients could be divided according to the severity of their neurologic symptoms into severe, mild and symptom-free types. Four patients had severe symptoms of drowsiness, headache, malaise, fever and vomiting. Six patients had milder symptoms of headache, listlessness, anorexia and slight fever. The remaining 6 had no symptoms or signs of meningoencephalitis. An increase in the number of cells, usually of mononuclear types, occurred in all of the 16 patients but the height of the cell count did not correspond to the severity of the disease. The highest number of cells, 1250, occurred in 1 of the patients with mild symptoms of the complication. An increase in the protein content was noted in all of the spinal fluids but the cultures were negative and sugar levels were normal The conclusion was reached that involvement of the central nervous system was a frequent occurrence in mumps often without any symptoms suggestive of the condition, so that its presence could only be detected by a lumbar punc-

A group of 38 children with meningoencephalitis following mumps was observed by T L Birnberg ¹⁶⁹ Common symptoms of the complication were vomiting, headache and fever which developed 1 to 10 days after the onset of the parotid swelling. In 2 patients there had been no definite evidence of preceding parotitis. The most frequent clinical changes denoting meningoencephalitis were rigidity of the neck, positive Kernig reactions and occasional variations in the intensity of tendon reflexes and reactivity of the pupils. The cerebrospinal fluids were usually clear, were sometimes under increased pressure and contained from 6 to 980 cells, mostly lymphocytes. All of the patients recovered but headaches persisted in 1 child for a period of 3 months and a partial central deafness of 1 ear occurred in another child.

The occurrence of meningoencephalitis and orchitis without parotid swelling, observed by W. Harris and H. Bethell,¹⁷⁰ led them to believe that this disease is a generalized infection and that the term epidemic parotitis is not adequate for describing the illness Two young adults under their care developed signs of encephalitis with meningeal irritation followed in 2 to 5 days by orchitis. No involvement of the salivary glands took place. In 1 patient an increase in the number of leukocytes in the cerebrospinal fluid to 740, with 55 per cent lymphocytes, was noted. Both patients made complete recoveries.

Severe encephalitis following mumps occurred in a patient reported by R. C Stewart and P. Edwards. 171 41 years of age contracted orchitis on the eighth day of his attack of mumps and shortly thereafter had severe symptoms of headache, delirium, and con-The cerebrospinal fluid was vulsions under increased pressure, contained an increased amount of globulin, and 158 cells, mostly polymorphonuclear forms Following the intravenous administration of 25 per cent glucose solution, the convulsive seizures ceased and recovery over a period of weeks was complete

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NEWBORN

By ROBERT A. LYON, M.D.

Causes of Death

The etiology of a large number of neonatal deaths has been reviewed by E. L. Potter and F. L. Adair. 172 In a series of 17,728 infants born during a 6½-year period, 402 were stillbirths, a rate of 23 per 1000 live births, and 371 other infants died during the first 10 days of life, a mortality rate of 21 per 1000 live births. Definite pathologic conditions could be detected at autopsy in only 57 per cent of the group. Prematurity which accounted for more than half of the deaths was not often accompanied by any gross pathologic change. Important causes of death, in order of frequency were malformations, intracranial hemorrhage and anoxemia. In about 46 per cent of the fetal deaths there had been maternal complications other than the mechanics of labor Chief among these were toxenna and hemorrhage from premature separation of the placenta Less frequent were infections such as syphilis and abnormalities of the cord

The tables on pages 578 and 579 indicate the relationship of types of delivery to neonatal mortality and the causes of death found at postmortem examination

The relationship between neonatal mortality and disease of the mother has been emphasized by J S P Beck ¹⁷³ The clinical histories of the mothers of 25 mfants who were born dead, or prematurely or who died shortly after birth were correlated with the pathological findings at autopsy. In 3 mistances, death of the infant could be attributed to congenital abnormalities of the infant, in 5 mistances to difficulties of labor and in 1 to syphilis Of the remaining 16 mothers, 10 had had toxemia of

various degrees, and the other 6 had suffered from premature separation of the placenta, premature rupture of membranes, or vaginal bleeding. The autopsies of the infants showed various degrees of maceration, prematurity, atelectasis, aspiration of fluid, and lesions resulting from asphyxia. The author called attention to the necessity of vigorous treatment of all mothers who are below their optimal health, by the administration of antianemia drugs, vitamins, suitable endocrine preparations and the cautious use of narcotics and anesthetics during delivery. Every effort should be made to have at hand all the equipment for resuscitation of babies of such patients. It was suggested that the respiratory passages be cleansed before the cord was tied.

Erythroblastosis

Erythroblastosis of the hydrops type has been observed in one of every 2000 deliveries by L. M. Hellman and A. T. Hertig,174 while icterus gravis has occurred in 1 of every 1500 deliveries. Mortality rates were 100 per cent in the hydrops form and 503 per cent in the gravis types Congenital hydrops was noted in a total number of 15 infants born of 13 mothers Toxemia of varying degree occurred in 30 per cent of these mothers, which was a much higher incidence than in the clinic population as a whole. Whether this was a cause of hydrops or a result of disturbed metabolism is a debatable question. Icterus gravis developed in 20 infants and the survey of the family histories of some of the patients gave no evidence that the disease had any hereditary characteristics. In subsequent infants of the

TABLE 5--(AUSEN OF DEATH ASSOCIATED WITH TYPES OF DELIVERY

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u u	Total, Per Cent	12.5	44 6	12.5	\$ 4	0 0	25 0	100 0
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	Neonatal Deaths	∞∞	112 112 7 7 2 3	4	<i>m m</i>	010	25 25 7 12 6	62
	Total, Per Cent	15 0	20 8	9.2	1.5	0 0		100 0
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		Hemorrhage Intracramal Intracramal and pneumoma Visceral	Anoxemia Maternal complications Abruptio or placenta praevia Abruptio and toxema Toxema Cord complications Medical complications No maternal complications	Malformations	Infections Preumonia Syphilis Septicemia Diphtheria	Idiopathic conditions Edema of the brain	No pathologic changes Maternal complications Abruptuo or placema praevia Abruptuo and toxemia Toxemia Cord complications Medical complications Syphilis No maternal complications	Total

(Potter and Adair J A M. A)

TABLE 0-(1005) OF OF DEVIEW AS DEMONSTRATED AT AUTOPSY OF 526 FETUSES AND INFANTS

Num- Per Nu		Истогице	rh igi	Vnoxemta	mta	Maltormations	attons	Intections	Suoi	Miscellaneous	aneous	Undete	Undetermmed	\mathbf{T}_{C}	Total
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	Total	*	15.8	10	18.5	95	181	16	5.0	6	1.7	776	430	\$26	100 0

(Potter and Adair: J. A M. A)

same families, congenital hydrops occurred in 50 per cent and icterus gravis in 80.3 per cent of the respective groups.

The possibility of making a diagnosis of erythroblastosis of the hydrops type in the fetus *in utero* by means of roent-genograms has been suggested by L. M. Hellman and F. C. Irving ¹⁷⁵ In 2 or 3 such cases observed by the authors there was an edema about the scalp which produced a corona in roentgenograms of the infant's skull. The value of making such an early diagnosis in order to insure early and adequate treatment is evident and such a routine procedure would be especially practical in all cases in which mothers have had previous infants with erythroblastosis.

Infections

The incidence of thrush in the newborn seemed to be related to vaginal mycotic infections in the patients studied by P. W. Woodruff and H. C. Hesseltine 176 Routine cultures of the vaginal mucosa of 402 women were taken during the last trimester of pregnancy and 28 per cent of the group were positive for fungi. The incidence of positive cultures was higher in women of the lower social and economic levels than in women in higher stations of life. Among 14,640 consecutive deliveries, thrush developed in 90 infants, an incidence of 06 per cent Of the 47 mothers known to have mycotic infections of the vaginal tract, 10 had infants with thrush infections of the mouth, an incidence of 21 per cent. The chances of an infant's contracting thrush were 35 times greater when the mother was known to have such vaginal infection than in the average maternal pop-There were 22 mothers of 49 thrush-infected babies who had had positive vaginal cultures and 27 who had no such infections. It seemed probable that many infants with oral thrush had contracted the disease, during delivery, from the vaginal tract.

Excellent results in the treatment of gonorrheal ophthalmia with sulfanilamide have been reported by M. W. Michels.¹⁷⁷ Fifteen children between the ages of 5 days and 3 years had been treated with this drug, and the results in this group were compared with those obtained in a series of 36 children treated with boric irrigations, the instillation of silver compounds, atropine sulfate and the application of ice compresses. The sulfanilamide was administered by mouth in doses of 1 grain per pound (140 mg per kg) of body weight daily. together with equal amounts of sodium bicarbonate. The series of patients treated with sulfanilamide remained only 58 days as an average in the hospital compared with an average of 285 days of the control series. Improvement of the eyes was more rapid and there were no complications from the therapy. The rapid response of such infections may prevent the disease from invading the cornea

 Λ technic for the prevention of gonorrheal ophthalmia in the newborn which has proved successful in more than 10,000 successive cases without any occurrence of the infection, has been reported by A. J. Skeel 178. The treatment consisted of the instillation of 3 or 4 drops of a ½ per cent silver nitrate solution into the eyes shortly after the cord has been tied. The lids were massaged gently for 45 seconds and then the eyes were irrigated with a 20 per cent solution of a mild silver protein. This routine therapy was repeated on 3 successive days Boric acid or mild silver solutions seemed to be ineffective in killing the organisms

Sepsis occurring in 27 newly born infants within a period of about 1 month has been reported by M L. Blatt and

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A. A. Wolf.¹⁷⁹ The infection occurred in nurseries in which 227 other infants had been born and had remained well during the same period of time. Common symptoms of the disease were loss of appetite and failure to gain weight. Mild diarrhea and fever occurred in some instances, and bronchopneumonia others, and the 7 infants who died had had symptoms of severe toxemia. autopsy, bronchopneumonia was found in 6 cases, enterocolitis in 2, multiple abscesses in 2, and endocarditis in 1 A variety of bacteria were obtained from these lesions. There was no evidence that the infection had been carried by the personnel of the institution or that contamination from the food or surroundings had been responsible for the disease. Only by closing the nursery for a period of 2 weeks was the epidemic checked successfully

The epidemics of diarrhea occurring in the newborn in New York City during the past 4 years have been summarized by S Frant and H Abramson, 180 Among 5082 babies exposed, 750 (147 per cent) contracted the disease and 356 died (475 per cent of the group affected). Although no definite bacterium or virus could be detected in these infants, the disease seemed to be a distinct entity because of its epidemic features The first infant affected often passed unnoticed at the beginning of an epidemic because of the slow onset of symptoms, but as each epidemic proceeded, the attacks became more severe and the symptoms developed more rapidly occurred within 7 days after the onset as an average

In a discussion of the methods of reducing the occurrence of infections, especially the epidemics of severe diarrhea in newly born infants, M L Spivek¹⁸¹ concluded that the best plan would be 1 of the dispersion methods of newborn care

to keep each infant isolated from other infected persons. This could be accomplished by the provision of (a) cubicle units; (b) small nurseries equipped to care for only 3 or 4 infants; (c) a small nursery for the individual baby in or adjacent to the mother's room; (d) hospital delivery and discharge to the home within 48 hours; or finally, (e) home delivery.

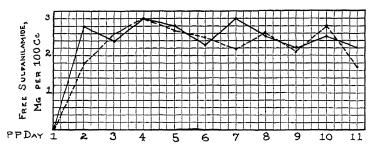
Placental Transmission of Minerals, Vitamins and Drugs

Maternal iron deficiency may have some effect in producing anemia of the offspring. The experiments of H. L. Alt¹⁸² have indicated that the deprivation of iron in female rats caused a depletion of the iron stores of their offspring although hemoglobin levels remained normal. Second litters of these rats had a diminution of the hemoglobin values and a reduction of the total amount of iron to one-fourth of its usual Animals receiving the iron-free diet lost some of the iron stores of the liver and during their second pregnancy developed a moderate anemia. It is questionable whether the results of such animal experiments can be applied to human conditions, but there have been some clinical observations which indicate that iron deficiency anemias of mothers are followed by decreased hemoglobin values of their newly born infants.

Variations in the vitamin C levels in the newborn are dependent upon the different amounts of the vitamin in the blood serum of their mothers. A W Fleming and H N. Sanford¹⁸³ found that average vitamin C levels in a group of 105 mothers was between 0.75 and 0.88 mg per cent. Each infant tended to have the vitamin in amounts which corresponded very closely with that of his mother. The level in the mother seemed to depend entirely upon the amount of

vitamin C ingested during the prenatal period. There was no correlation between the amount of vitamin C in the mother's blood and the birthweight of her child, the amount of milk secreted or the rapidity of weight gain of the nursing infant. Mothers must continue to ingest the vitamin after delivery in order to maintain at normal levels the amounts secreted in the breast milk. A group of 7 infants with evidence of cerebral hemorrhage had amounts of vitamin C in their blood of less than 0.62 mg per

The blood of the infants of the above group of maternity patients contained slightly larger amounts of the vitamin than their mothers and the levels in the cord blood were considerably higher than those in either the infant or maternal blood. The ascorbic acid in the blood plasma of the infants tended to decrease within 24 hours after birth and reached levels comparable to those of maternal plasma within 10 days unless ascorbic acid was given by mouth. Capillary resistance of the infants followed a similar



CHARI 1—Free sulfamilamide in the blood and milk of a mother on 60 giains (4 Gm) of sulfamilamide daily. Blood indicated by solid line, milk by broken line. On a uniform dosage with normal renal function, the sulfamilamide concentrations in the blood and milk are closely parallel (Stewart and Pratt. J. A. M. A.)

cent which was lower as an average than the figures for normal infants. Although none of the infants had clinical scurvy, it seemed advisable to maintain the concentration of vitamin C at high levels by the administration of it to mothers during the prenatal period.

The levels of ascorbic acid in the plasma of 23 women shortly after delivery were very low (average, 0.26 mg) in the tests made by P. W. Braestrup 184. It seemed probable that the diets of the majority of the women had been low in vitamin C. Women on other wards of the hospital, who were ill, had levels almost as low as the maternity patients, while a group of healthy women were found to have much higher levels but not as high as the group of women who received large amounts of ascorbic acid daily.

course and tended to decrease during the first 10 days of life but discrepancies arose in individual cases so that there seemed to be no definite relationship between this condition and the plasma ascorbic acid content. Some other vitamin may have a more direct influence upon capillary resistance.

Determinations of the ascorbic acid content of plasma in the newborn on various diets have been made by R L Mindlin ¹⁸⁵ Average levels in 21 infants nursed on the breast were 10 mg per cent. A second group of 19 infants who were given artificial feedings of pasteurized milk, water and Karo for about 1 week, had much lower amounts of the vitamin (04 mg per cent). The administration of ascorbic acid to a group of 10 infants fed like those of the second series, maintained levels of the vitamin

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comparable to the breast-fed infants. It was the conclusion of the author that vitamin C should be administered to all infants as soon as they are given artificial feedings and one should not wait until the age of 2 or 3 months as has recommended frequently.

The levels of vitamin C in the blood plasma of pregnant women was 0.6 mg. per cent as an average during the first

is 2 weeks of age was emphasized and if mothers nursing their infants do not seem to be taking an adequate diet, the vitamin must be given to them also.

Sulfanilamide administered to mothers of newly born infants was excreted in the breast milk in concentrations very similar to that occurring in the maternal blood. These observations were made by H. L. Stewart, Jr., and J. P. Pratt¹⁴⁸ in

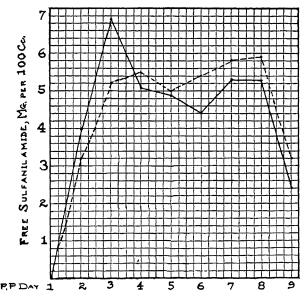


CHART 2—Blood indicated by solid line, milk by broken line. In contrast to the first group (Chart 1), concentration of sulfamilamide in the milk was generally equal to or slightly higher than the blood. Drug discontinued on the eighth day. (Stewart and Pratt J. A. M. A.)

5 months in the series observed by C E Snelling and S. H. Jackson. 186 A gradual decline occurred until the ninth month when the averages were 0.42 mg. per cent After delivery only 023 mg were present. The cord blood levels of the vitamin were higher than those of the mothers. Breast-fed babies had adequate amounts of plasma ascorbic acid if the milk contained as much as 4 mg per cent Artificially-fed infants did not derive enough vitamin C from their feedings and their plasma levels were only 0.19 mg per cent as an average. The necessity of adding vitamin C to the diet of an artificially-fed baby by the time it

a group of 10 mothers who received daily amounts of 30 grains of the drug and in a second group of 10 who received 60 grains a day. In the first series, the amount of sulfanilamide in the blood and milk reached levels of 2 to 4 milligrams per cent. In the second series in which the mothers received double amounts of sulfanilamide, the concentrations rose to 4 to 7 milligrams per cent. The babies of both groups made satisfactory gains in weight, took an average amount of breast milk, and were normal in every respect. Small amounts of the drug appeared in the blood of the infants and 1 to 26 milligrams per cent were excreted in the

urine during a 24-hour period. No toxic effects of the drug were noted in the infants. When the administration of the sulfanilamide to the mothers was discontinued, the amount excreted in the milk decreased rapidly. It would seem impossible to raise the concentration of sulfanilamide in the breast milk to such levels that the infant could obtain therapeutic doses by this method. When the sulfanilamide was given to a group of mothers during labor, the cord blood and

than 0.12 Gm. of the drug during that time and this would never be harmful except in the few rare instances in which an infant was especially susceptible or allergic to sulfanilamide.

Prematurity

The *incidence* and some of the *predis*posing causes of prematurity have been reviewed by C. H. Peckham. When the weight of 5.5 lbs. (2500 Gm.) was considered as the borderline between

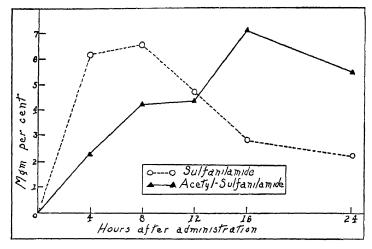


Fig. 3—Excretion of sultanilamide and acety-sulfanilamide in human milk (Pinto J A M A)

ammotic fluid were found to contain small amounts of the drug

The excretion of sulfanilamide in human milk has been observed by S. S. Pinto 187 Sixty grains of sulfanilamide were administered in 3 doses over a 2hour period in the morning. The concentration of the drug in the milk reached its height within 8 to 12 hours. The conjugated sulfanilamide reached its peak of concentration in the milk several hours later More than half of the amount of drug administered was eliminated through the kidneys Even though the blood levels of the sulfanilamide were maintained at 10 mg. per cent in the mother during a 24-hour period, the nursing baby would probably not receive more premature and full term deliveries, the incidence of prematurity was found to be 9 19 per cent of a total of 39,394 live births. When only the infants less than 45 cm in length were considered as prematures, the incidence dropped to 5 55 per cent. Negro infants were considerably lighter and shorter than white infants. In the case of twin deliveries, there was a tendency for the heavier baby to be born first.

There was no evidence to support the theory that frequent pregnancies led to premature births. The incidence of prematurity did not increase with advancing maternal age, although the incidence of small infants was a little greater in women over 35 years of age. There were

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more female than male premature infants. Prematurity was noted a little more frequently among first born children, but this may have been only a physiologic tendency for the young mothers to have small infants.

Prematurity occurred only slightly more frequently when the membranes ruptured prematurely but was definitely more frequent when maternal disease, such as syphilis, heart disease, eclampsia, and placenta previa, were present. Operative procedures were about as frequent in premature births as in the full term infants

The true incidence of prematurity did not seem to be reflected in these studies. The criteria of weight and length seemed to omit factors of race, sex, age, and parity. Some correlations of the above influences with height and weight and the inclusion of the term of pregnancy might give a clearer picture of the true incidence.

The mortality rates of the same group of prematures were subjected to analysis by C H. Peckham 189 Death and stillbirth rates were high for infants weighing less than 264 lbs. (1200 Gm.), but declined rapidly for infants weighing 4 to 5 3 lbs. (1800 to 2400 Gm.) Stationary levels were reached by infants more than 6 lbs. (2700 Gm) in weight and 18 in (47 cm.) in length Mortality rates were higher in the prematures born singly rather than as 1 of a multiple pregnancy, were higher with the advancing age of the mother; increasing parity; and in the male infants. Stillbirth rates of negroes were higher but mortality rates of living infants were lower than those of the white race Of little or no effect on the mortality or stillbirth rates was the birth order in the case of multiple pregnancies, the time of the rupture of membranes, the type of delivery or the anesthetic employed.

The conclusion was reached that multiple influences may be exerted as the cause of prematurity and early death. Each case has problems of a specific kind. It would seem advisable to prevent excessive uterine contractions, avoid the use of forceps and operative methods, and use as little anesthesia and analgesia as possible, in order to reduce the death rates of this type of infant.

The progress of 96 premature infants during 6 to 18 subsequent years of life was reported by W. Schoberlein. 190 The average birth weight of these infants was 3.7 lbs. (1690 Gm.). From the histories obtained from the mothers, the school teachers, and from examinations of the patients, about one-fourth of the group were found to compare favorably with normal infants born at term. A large percentage of the premature infants had been somewhat slow in learning to walk and to establish normal toilet habits. There was a nervous and emotional instability in larger percentages of those born prematurely than in normal groups of children Forty per cent were nervous, 63 per cent were unable to concentrate upon school work, 55 per cent tired easily, and 13 per cent had trouble in getting along with their associates. The heights of the children born prematurely were approximately the same as those of normal children, but the weights of the former group were below the normal. Certain physical defects such as strabismus and undescended testes were more frequent than normal in the premature group The intelligence levels of prematurely born children varied in relation to their birth weights. The heavier premature infants had higher intelligence quotients as a rule than the lighter ones and only among those whose birth weights were above 3.3 lbs. (1500 Gm.) were there instances of superior achievement in school In the group of children with

birth weights of less than 3.8 lbs. (1750 Gm.) there was a higher percentage of mental deficiency. The fate of premature infants could not be predicted at birth and their physical and mental status had to be determined from long periods of observation and examination

The subsequent course of a group of 152 prematurely born infants was compared by R. S. Illingworth¹⁹¹ with that of the same number of normal infants weighing 8½ lbs. (3860 Gm.) or more at birth. The percentage of premature infants who were underweight in the later years of childhood was much higher than that of the children born at term. The mean difference in weight between the 2 groups in later years was 4.2 to 17 1 lbs (1900 to 7772 Gm.). The incidence of infectious diseases was approximately the same in the 2 groups of children but allergic diseases, such as eczema, were observed more frequently in infants who were heavier at the time of birth. Spastic diplegia, gross mental deficiency, and convulsions occurred more frequently in the children born prematurely than in the full term infants was difficult to determine whether the differences between the 2 groups of infants was entirely due to the length of gestation. Some of the conditions predisposing to prematurity, such as malnutrition of the mother, may have been due to madequate diets and some of these similar nutritional factors might have affected the infants during the early vears of life.

The weight gain of a group of premature infants has been considerably accelerated by the daily administration of yeast H R Litchfield, J Lichterman, I. Knoll and I. Kurland¹⁹² employed a yeast extract which had a potency of 100 international B-1 units and 40 Sherman B-2 units per teaspoonful. A dosage of 1 teaspoonful twice daily in orange juice

was administered until favorable weight gains occurred and then the dosage was decreased. A series of 58 infants were treated in this manner and 52 untreated infants were observed as a control group. All of the premature infants received the usual care given patients of this type. The infants who received the yeast began to gain earlier and added more weight than the control series. Fifty-five per cent of the treated infants began to gain during the first week of life as compared with only 8 per cent of the control group. At the end of $2\frac{1}{2}$ weeks, 95 per cent of those who had received the vitamin had gained in weight as compared with 48 per cent of the control group. At the end of 3 months the treated infants whose initial weight was less than 3.3 lbs. (1500 Gm.) had gained 4 or 5 times their birth weight, while those who were not treated gained only 2 or 3 times their birth weight. Similar results were noted in the heavier infants. No complications or gastric upsets followed the administration of this vitamin. The administration of the vitamin B may have assisted in the retention of body fluids or may have had some indirect influence upon other factors which stimulate growth.

On the assumption that some cases of prematurity may be the result of a vitamin E deficiency of the mother, this vitamin has been administered as a therapeutic measure to premature infants by F. Widenbauer¹⁹³. Wheat germ oil was administered to 17 infants and rapid increases in weight at greater than average rates occurred in 11 of the group

Respiratory Diseases

Pure oxygen seemed preferable to mixtures of oxygen and carbon dioxide in the resuscitation of experimental animals with anoxemia studied by N J. Eastman, R. B. Dunn and J Kreiselman. Anoxemia was produced in

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dogs by the administration of 100 per cent nitrous oxide which caused symptoms and changes identical with those observed in infants with asphyxia neonatorum. The first symptom was a tendency to breathe more rapidly to secure additional oxygen supply, and an increase in the heart rate to supply tissues with oxygen. Then, as the oxygen supply of the blood was reduced, there were loss of consciousness, bradycardia, apnea, limp extremities, relaxed sphincters and a white, cold skin similar to that of a patient in shock.

In restoring normal conditions in the animals, pure oxygen mixtures brought about recovery as quickly as did mixtures of oxygen and carbon dioxide. The oxygen was more efficacious in animals in severe stages of asphyxia and as recovery occurred, normal respiratory rhythms were restored more readily with the oxygen alone. The presence of carbon dioxide in the inhaled air seemed to have a toxic effect and made the respiratory movements convulsive in type and irregular in rhythm Carbon dioxide concentrations of 25 per cent led to severe reactions and sometimes death.

.1pnea of the newborn seemed to bear a definite relationship to the administration of analgesic to the mother during labor in the series of patients reviewed by F. Schreiber 195. The term apnea was employed in all instances in which respiration was delayed or some type of asphyxia was present so that resuscitation was required. Of a series of 500 infants with apnea, 155 had precipitous, breech, twin or premature deliveries. In most cases the apnea occurred at the time of birth but in 11 per cent it occurred later and in 18 per cent the apnea was noted at birth and again later in the infant's life Analgesics seemed to depress the respiratory center and produce cerebral anoxemia.

Pneumothorax in a newly-born infant has been reported by H. Strongin. 196 The chief symptoms were a rapid respiratory rate, an absence of breath sounds and a hyperresonant percussion note over the affected side. The final diagnosis was made by roentgenograms. Treatment of the patient consisted of the removal of air from the pleural cavity on 2 occasions and this was followed by complete recovery of the infant. Trauma at birth seemed to be the cause of the condition and this has been the chief etiologic factor in the 28 cases previously reported in the medical literature. Pneumothorax must be differentiated, in the roentgenologic or fluoroscopic examination, from congenital cystic lesions of the lungs.

Skin Lesions

The treatment of vascular birthmarks has been reviewed by F. Young. 197 The commonest type of birthmark is the capillary hemangioma or port-wine stain. Many of these birthmarks are small and occur at the back of the head, the nape of the neck, on the front of the forehead, or at the base of the nose Many of these marks disappear spontaneously. When the port-wine stains are more extensive, the type of treatment is more varied and none of the forms of therapy are entirely satisfactory. Radium or roentgen therapy and carbon dioxide snow are agents commonly employed but they often leave some disfigurement from scars. When the marks are small, surgical excision may be tried either by removing a part of the lesion at a time or by completely removing the stain and grafting with a full skin graft. Blistering doses of ultraviolet irradiation have recently been reported as a successful method of treatment.

The second type of birthmark, the hypertrophic endothelial hemangioma, may

readily be removed by surgical excision if the growth occurs on the trunk or extremities. When it is on the face it may be necessary to employ radium or roentgen ray therapy, or electrodesiccation. These latter methods must be used with care about the face.

The third type of birthmark, the cavernous hemangioma, is more difficult to remove and in this case the injection of a sclerosing material is probably the most successful because it eradicates the hemangioma without injuring the overlying skin. Electrocoagulation has also been used for this type of tumor. The treatment in all 3 forms of birthmarks depends considerably upon the extent of the lesion and its location, so that judgment must be used in applying the various forms of therapy.

Tetany of the Newborn

Tetany of the newborn has been reviewed by H. Bakwin ¹⁹⁸ The chief clinical manifestations of the disease are convulsions and twitchings, a hypersensitivity to noises and other stimuli and exaggerated facial and peroneal reflexes. Carpopedal spasm is rarely observed at this age. The diagnosis is established by finding a serum calcium level of less than 8 milligrams per cent. The prognosis is generally good.

The cause of tetany in the newborn probably differs somewhat from that in older infants. In the latter group tetany seems to be related to deficiency of vitamin D, and recovery will follow the administration of that vitamin. This is not true of tetany in the very young infants who respond best to the administration of calcium. In the newborn there is a tendency for the serum calcium levels to fall shortly after birth and during this time small amounts of phosphorus may be found in the urine. It has been suggested that a physiologic

hypoactivity of the parathyroid glands occurs in many of these infants.

In their studies of serum calcium in the newborn, B. S. Denzer, M. Reiner and S. B. Weiner¹⁹⁹ found that the calcium content of the cord was generally higher than that of the mother's blood, and that there was a tendency for the serum calcium levels of the infant to drop during the first few days of life. A rise in calcium began about the tenth day of life in both the white and negro infants. The extent of the primary fall of the calcium content did not seem to be related to the infant's birth weight, the type of feeding or the amount of weight lost during the first few days of life When the cord blood contained large amounts of calcium, the fall was usually greater than in the case of infants with lower levels of calcium in the cord blood. In none of the patients studied did the calcium fall as low as the tetany zones. No correlation could be found between the serum calcium and protein content of the blood Phosphorous levels rose during the first week of life so that the average amounts for the first 4 days were 6.7 mg per cent and for the succeeding 4 days 7.1 mg per cent. Infants with low calcium levels did not have phosphorus in amounts greater than the average Variations in the technic of performing the tests for phosphorus would account for considerable variation in the results reported by different investigators. The authors were unable to find any definite evidence that the temporary depression of the parathyroid gland secretion was responsible for the variations in calcium during the first few days of life, although they did not deny that such a condition might occur

Blood calcium and phosphorous levels of the newborn have also been studied by W. R Todd, E G. Chuinard and M. T. Wood.²⁰⁰ Specimens of blood

were obtained from fontanelle punctures on the first to third day of life of 693 infants and in a smaller group on the fourth to seventh day. The average calcium level was 10.15 mg. per 100 cc. with a range from 7.2 to 13.9 mg. The levels were a little higher as an average in the autumn or winter than in the other seasons of the year. The sex and weight of the infant and the age of the mother had no influence on the calcium content of the infant's blood. Parity, however, seemed to exert some influence since the infants born of mothers who had had 3 or more children previously, generally had significantly lower levels of calcium.

Averages for blood phosphorus were 6.03 mg. per cent and were somewhat higher in the spring months than in other seasons but were not affected by the sex and weight of the infant or by the parity of the mother.

Blood taken later in the first week of the infants' lives generally contained more calcium and less phosphorus than immediately after birth. Venous blood obtained by fontanelle puncture gave more accurate values of the calcium and phosphorus of the infant than did the cord blood.

Weight Loss

Some factors influencing the weight loss of the newborn during the first week

of life have been reviewed by W. C. C. Cole.²⁰¹ He first determined the average weight loss and subsequent gain during the first 8 days of life, of 996 normal infants. The average maximum weight loss of 5 per cent of the birth weight occurred on the third day and by the eighth day the average baby was 1.33 per cent below his birth weight. The trend of the weight curve of infants of primiparae was about the same as those of multiparae. The drop in weight was found to be less than average in (a) infants delivered by version or by cesarean section, (b) breech presentations, (c) deliveries in which labor lasted for more than 24 hours, (d) instances in which ether anesthesia had been given the mothers for more than 1 hour, and (e) infants whose cords had not been tied until pulsation had ceased. When drugs such as amytal were given to the mothers, the infants' weight loss was less than average but scopolamine and morphine administration was followed by greater than average weight loss of the infants Pituitrin given to the mother had but little effect on the weight curve of the infant except to retard the recovery of weight by the end of 8 days The author questioned the validity of the term "physiologic weight loss" of the newborn since several obstetric factors seemed to influence this curve.

NUTRITION AND NUTRITIONAL DISEASES

By Waldo E Nelson

Vitamin A

The question of toxicity of vitamin A has been raised on several occasions by investigators working with animals. The observations of E B Vedder and C. Rosenberg²⁰² indicate that if vitamin A is ever toxic, it is in doses in excess of

100,000 international units daily for 50-gram rats

The amount of Vitamin A contained in cod-liver oil averages about 1800 international units per grain and the daily requirement of infants is estimated at 3000 to 5000 units.

Vitamin B₁

Two cases of acrodynia which showed dramatic improvement within 3 days after beginning intramuscular injections of vitamin B₁ are reported by J. I. Durand, V. W. Spickard and E. Burgess 203 In each instance the improvement ceased and the symptoms grew worse when these injections were discontinued and the vitamin was given by mouth. In view of the report that vitamin B₁ was not absorbed in cases of achlorhydria, a gastric analysis was done in the first case and both free and combined hydrochloric acid were found to be present in average amounts The first patient was also given nicotinic acid for a period of 2 weeks but this was started after marked improvement had been made, and it was doubted that recovery was hastened. In spite of the relapses which occurred when treatment by mouth was tried, both patients had recovered in 6 weeks from the beginning of injection treatment. The authors believed that this period might have been greatly shortened had the intramuscular administration been given continuously at 2to 3-day intervals

Vitamin C

Ascorbic Acid—According to I S Wright,204 4 general statements may be made concerning the present status of ascorbic acid (1) Most cases of scurvy can be cured with ascorbic acid. A few appear to be resistant to this substance whereas they can be cured with large amounts of lemon or other citrus fruit (2) Increased fragility of the capillaries when due to vitamin C deficiency will be restored to normal by the use of ascorbic acid, with the same exception as noted (3) Vitamın C deficiency may occur under a great variety of conditions even when the intake of this substance is apparently adequate These include in-

creased metabolism from infection (with or without fever) or from other causes. interference with absorption or utilization because of achlorhydria, colitis or other intestinal disturbances and additional factors concerning which our present knowledge is limited. Deficiency inevitably occurs in man when the intake is inadequate, since man is apparently unable to synthesize this substance and his storage capacity is very limited. (4) The proved indications for vitamin C therapy depend primarily on the presence of or danger of a deficiency of this substance in the patient. This applies whether the primary problem is clinical or subclinical scurvy or any of the very numerous diseases for which it has been recommended as an important therapeutic aid.

The data of C. E. Snelling and S. H. Jackson²⁰⁵ indicate that there is a slight fall in the ascorbic acid content of the plasma of pregnant women toward the end of pregnancy The fetus is said to act as a parasite and has higher plasma levels of ascorbic acid than maternal blood taken antepartum. Totally breastfed babies were well supplied with vitamin C, if the ascorbic acid of the milk was greater than 4 mg per cent, if the ascorbic acid was below 2 mg per cent in the breast milk, there was likelihood of deficiency in the baby. In artificially fed babies not receiving additional vitamin C, the level of ascorbic acid was low

The authors make the following recommendations. Artificially fed babies should receive additional vitamin C from the time they are 2 weeks of age. The mothers of breast-fed babies should have adequate vitamin C in the diet, and if there is any question of lack in the mother's diet, the babies should receive additional vitamin C.

Vitamin C and Lactation—T. H Ingalls, R. Draper and H M. Teel²⁰⁶

have studied vitamin C metabolism during lactation. Fresh breast milk from mothers on the usual diets of a maternity ward was found to contain an average of 4.5 mg ascorbic acid per 100 cc. during the first two weeks of lactation. Breast-fed babies of these mothers received an average of 28 mg. of ascorbic acid daily. When a liberal amount of vitamin C (300 to 600 mg. daily) was added to the mothers' diet, ascorbic acid content of the breast milk increased to 7.3 mg. per 100 cc. The babies of such mothers received an average of 46 mg. of ascorbic acid daily.

Since the concentration of ascorbic acid in human milk was found to be considerably greater than that in blood plasma, it was suggested that ascorbic acid is secreted rather than diffused into the milk.

Vitamin C nutrition in nursing infants is thus shown to be contingent on the ascorbic acid content of breast milk, which is in turn influenced by the vitamin C intake of the mother. The increased maternal need for vitamin C which was demonstrated to exist during pregnancy persists during the nursing period.

Distinct differences between the plasma ascorbic levels of breast-fed and artificially fed newborn infants has been shown by R L Mindlin 207 The plasma ascorbic acid concentration of normal 2-week old infants on breast feeding averaged 10 mg per cent. The plasma ascorbic acid concentrations of normal 2-week old infants on artificial feedings for about 1 week averaged 0.4 mg. per cent Lower values resulted from longer periods of artificial feedings. It was shown that addition of sufficient ascorbic acid to the diet prevented the fall in plasma concentration invariably found with pasteurized milk feeding.

In contrast to the findings of Ingalls and his co-workers are those of A. W. Fleming and H. N. Sanford.²⁰⁸ In a comparison of 72 mothers and their infants, it was found that the amount of vitamin C in the infant's blood was directly determined by the mother's blood vitamin C value and the infant's blood was on the average similar to that of the mother. The average vitamin C level of the mother's plasma was 0.884 mg. per cent and that of the infant's was 0.753 mg. per cent. The amount of vitamin C in the mother's blood is said to have had no influence on her production of breast milk, on the gain or loss of the infant, or any influence on the infant's birth weight. The birth weight of the infant was not influenced by the amount of its blood vitamin C. However, it is stated that if the mother has an average amount of blood vitamin C, a gain in weight by the infant taking her breast milk is followed by a small gain in the infant's vitamin C blood content.

The observations of B. M. Hamil, L. Reynolds, M. W. Poole and I. G. Macy²⁰⁹ indicate that the minimal protective dose of vitamin C for the average healthy infant is about 10 mg. per day. The optimal dose is, of course, somewhat above this amount

Ascorbic Acid in Tissues—Studies on the concentration of ascorbic acid in the tissues have been carried out by T H Ingalls ²¹⁰ Ascorbic acid concentrations in the livers of 70 infants coming to autopsy were determined and the results correlated with the dietary history and the histology of the rib. At birth, the amounts of ascorbic acid were uniformly high, ranging between 20 and 75 mg per 100 Gm of liver. From birth to 1 month, both mean and extreme values were significantly lower, although in only 1 instance was the figure less than 10 mg per 100 Gm of tissue. There-

after, 18 of 45 patients between the ages of 4 and 26 months showed concentrations of ascorbic acid in the liver below 10 mg. per 100 Gm. The low values for ascorbic acid could be correlated more closely with the dietary intake than with the type and degree of infection Patients with histologic evidences of scurvy in the rib showed the lowest concentration of the vitamin in the liver, averaging less than 5 mg. per 100 Gm. of tissue.

Distribution of ascorbic acid between cells and serum in relation to excretion of it in the urine has been studied by M. Heinemann.²¹¹ In fasting blood, a general correlation was found to exist between the ascorbic acid concentration in cells and in serum. The concentration in cells consistently exceeded that in serum Concentrations greater in serum than in cells were observed transiently following absorption of ascorbic acid, when the exchange between vitamin C in serum and cells caused fluctuation in their concentrations These fluctuations were more marked in both cells and serum than in their resulting whole blood The whole blood concentration of ascorbic acid appeared to correspond almost lineally to the degree of saturation of experimental subjects. It also closely indicates the different phases of complete saturation produced by test doses of ascorbic acid, as measured by the amount excreted in the urine Serum and whole blood concentrations were only roughly correlated. The determination of ascorbic acid in whole blood thus appeared to be preferable for practical purposes.

Urinary Elimination of Ascorbic Acid—The urinary elimination of large amounts of ascorbic acid, following intake of a test dose by saturated subjects, depended on its concentration in the tubular reabsorption. The relation between the curve of excretion and the

concentration in cells and serum suggested that the rate of absorption by the tubule cells may depend upon the concentration of ascorbic acid in these cells

It was found that ascorbic acid is taken up from the plasma by red cells both *in vivo* and *in vitro* at a slow rate.

The mechanism of the excretion of vitamin C by the human kidneys has been studied by E P. Ralli, G. J. Friedman and S H. Rubin ²¹² Simultaneous vitamin C and inulin clearances showed that vitamin C was excreted by filtration and by active tubular reabsorption. The reabsorptive mechanism for vitamin C appeared to be limited by a maximal rate, so that when the vitamin was presented to the tubules by the glomerular filtrate at a rate exceeding this maximum, the excess was excreted in the urine The excretion of vitamin C in a given individual appears to be determined by (1) the plasma level, (2) the rate of glomerular filtration, and (3) the maximal rate of tubular reabsorption. The nature of the reabsorptive process is such that at low plasma levels the vitamin C clearance reaches a minimal and constant value. The authors conclude that, although in chemical structure, vitamin C is related to carbohydrates, it is not reabsorbed by the same mechanism as glucose

Vitamin C Metabolism in Tuber-culous and Normal Children—Further data on vitamin C metabolism in tuberculous and normal children have been supplied by T. S Bumbalo and W. W. Jetter ²¹³ The urinary excretion of vitamin C was determined in 2 groups of tuberculous and normal children, respectively The children in each group received approximately the same basic vitamin C diet of 55 to 65 mg daily After the initial period of observation, 50 mg of synthetic vitamin C was added to the daily diet of each child. An imme-

diate rise was noted in the urinary excretion of vitamin C in the normal group, whereas the tuberculous group, in whom the average basic excretion was 6.4 mg. per 24 hours, required an average of 750 mg. in 15 days to produce a rise in excretion to 10 mg. per 24 hours. The maximum output of 23 mg. per 24 hours was obtained on the twenty-fourth day after 1200 mg. had been ingested. Subsequent feeding produced no further Upon discontinuance of the increase added vitamin, the excretion of the tuberculous group promptly fell to the previous subnormal levels. The added need of vitamin C during active tuberculous infection is emphasized by this study.

Vitamin D

Effect on Linear Growth in Infancy-Further studies on the effect of vitamin D on linear growth in infancy are reported by P. C Jeans and G. Stearns 214 The rate of linear growth of 9 infants given from 1800 to 4600 units of vitamin D daily was compared with standard rates of growth, and with the growth of infants given the same dietary regime but amounts of vitamin D varying from 135 to 340 units daily. The rate of growth with the very high vitamin D intake was similar to or less than those of infants given 135 units daily, and definitely lower than the growth rates of infants given 340 units of vitamm D daily. They conclude that the effect of vitamin D on increasing linear growth reaches a maximum when the vitamin D intake is greater than 135 and less than 1800 units, probably in the neighborhood of 340 to 600 units daily Vitamin A in amounts exceeding those in an adequate diet apparently does not affect the linear growth of infants

Antirachitic Effectiveness—An investigation has been carried out by J. M Lewis²¹⁵ to determine whether the anti-

rachitic effectiveness of a fish liver oil preparation, such as percomorph liver oil, is increased by dispersion in the daily ration of milk. The result of this study from a prophylactic standpoint reveals that, while both the emulsion and the oil (percomorph liver oil in ½ teaspoonful of orange juice) were effective antirachitic agents, the incidence of rickets was less in the group of infants receiving the emulsion in milk. In the curative tests similar results were obtained, in that the healing response was greater in those infants receiving the preparation of milk when compared with those receiving the oily solution. Analysis of the data revealed that the emulsion in milk was approximately twice as effective as the only preparation at the dosage level employed in this investigation.

According to H Vollmer,²¹⁶ rickets and tetany can be cured by peroral administration of 1 single dose of 600,000 international units of Vitamin D. It is said that the curative effect is more prompt than that obtained with the daily administration of small doses. Serum calcium and serum phosphorus become normal and roentgenographic evidence of calcification is visible within 1 week. The most impressive effect is the rapid rise of serum calcium. In 2 cases of tetany, convulsions did not occur after vitamin D shock therapy, and all other symptoms of hyperirritability disappeared usually occurs within 2 days without any additional therapy. Higher than normal values of serum phosphorus may occur after vitamin D shock therapy, but usually decline to a normal level in from 2 to 4 weeks The following conditions are suggested as indications for vitamin D shock therapy. Neonatal and infantile tetany; severe rickets, rickets associated with pneumonia or pertussis, rickets associated with chronic infections, and

indifference of the parents of a rachitic or tetanic child. There appear to be no contraindications. No toxicity was manifested in 150 children treated with massive doses of vitamin D. The proper dosage is said to be 600,000 international units, incorporated in milk.

Nonvitamin D Rickets Therapy—A. T. Shohl and A. M. Butler²¹⁷ report the healing of rickets in 2 infants following treatment with a mixture of citric acid and sodium citrate and without vitamin D. Aside from the theoretical interest, the authors point out that the cure of rickets by factors other than vitamin D is of specific interest in the treatment of rickets resistant to vitamin D, and perhaps in other disturbances of calcium and phosphorous metabolism

Vitamin D and Dental Caries -The rôle of vitamin D in the control of dental caries in children has been studied over a period of 4 consecutive years by E C McBeath and T. F Zucker 218 A seasonal incidence of dental caries was found to exist. The greatest incidence was found in late winter and early spring with very low values during the summer. Previous observations on the beneficial effects of vitamin D were verified. The administration of graded amounts of natural (animal source) vitamin D as vitamm D milk was successful in reducing the incidence of dental caries. Of the 3 doses of vitamin D administered (250, 400 and 800 international units per day) only the last named was adequate to prevent an increase during the height of the caries season above that of the previous period. Fortifying the diet with "protective foods" or simply increasing the allowance of milk in the diet led to a moderate reduction in caries when no appreciable vitamin D was added. This change was clear cut in the autumnwinter period but not so definite in the winter-spring period A reversal of "control" and "experimental" régime during 2 successive years in over 100 cases showed that individual susceptibility to caries was negligible as compared to the effect of nutritional factors.

Epiphyseal Rating

The employment of roentgenographic data of the ossification centers or the so-called epiphyseal rating as a measure of constitutional health is recommended by C. C. Francis.²¹⁹ It is pointed out that there is a definite sequence as well as date of appearance for centers of ossification, and that this schedule may be interrupted or retarded by metabolic or constitutional disturbances. Height, weight, bodily maturity and even mental expansion may show irregularities in progress. It is stated, however, that epiphyseal rating is the earliest and frequently the only indicator of nutritional disturbance Progress in epiphyseal rating may be used as a delicate measure of constitutional health in young children, but it will fail if employed as an indicator of bodily maturation. Sick children show a lag in epiphyseal rating proportionate to the duration and intensity of the constitutional disturbance When convalescence is completed, the epiphyseal rating advances again. The epiphyseal rating is also influenced by available mineral and vitamin D Children on a low mineral ration tend to lag in epiphyseal rating. As a corollary of this, children growing very rapidly will tend to lag in epiphyseal rating unless they are provided with ample rations of mineral and vitamin D When the period of rapid growth comes to a close the epiphyseal rating advances rapidly Children growing slowly and given a diet rich in minerals and vitamins, particularly vitamin D, tend to advance rapidly in epiphyseal rating. Figure 4 illustrates the dates of appearance of centers of

ossification in white boys from birth to 5 years of age.

Milk

Nutritional studies have been carried out by Lydia J. Roberts and her coworkers in an attempt to determine (1) whether the daily addition of a pint of deviation from average weight for height and age, condition of teeth, and the stage of osseous development as measured by the carpal development. One group remained on the usual institutional diet as the control (this diet is described as a rather mediocre institutional diet); 1

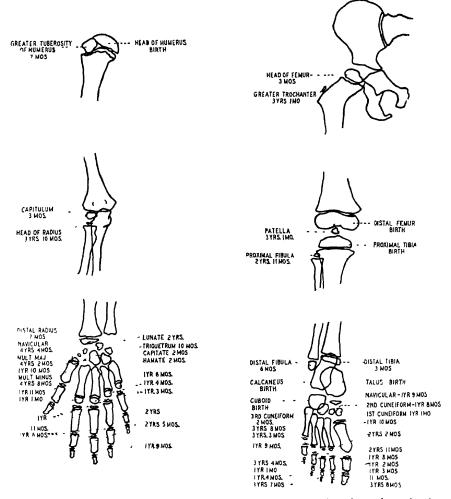


Fig. 4—Dates of appearance of centers of ossification in white boys from birth to 5 years of age. (Francis. Am. J. Dis. Child.)

milk to the diet of children already receiving approximately 1 pint would produce any measurable improvement in physical status over a period of 1 year, and (2) whether any advantage could be demonstrated for irradiated over non-irradiated milk. The children were divided into 3 groups, matched as closely as possible on the basis of age, sex,

received daily an additional pint of reconstituted evaporated milk, and 1 an equal amount of irradiated evaporated milk. In the first portion of the study²²⁰ the effect upon growth in height and weight was measured. Both groups receiving the daily addition of a pint of milk showed measurable increases in growth in height and weight. These dif-

ferences, however, were not large and did not always attain statistical significance. They did point consistently in the same direction and the authors felt that they probably represented real differences which could be attributed in part, at least, to the dietary supplement.

In the second portion of the study²²¹ the effect of these milk supplements upon the ossification of the bones of the wrist was measured The 2 groups receiving the milk supplement showed somewhat greater and statistically significant progress than did the control group. There was no significant difference between the 2 groups receiving milk All 3 groups at the outset were retarded in respect to the Carter norms of carpal development and were still retarded at the end of the study However, both groups given a supplement of milk reduced their deficit to a greater degree than did the control group.

In the third portion of the study²²² the effect of these 2 milk supplements on the development and spread of dental caries was observed. All the children showed extremely progressive caries. Although the difference in advance in caries between the groups was small and statistically insignificant, there was a consistent tendency according to all methods of comparison for the progress of caries to be slightly less for the children given a supplement than for the control children, with no consistent difference between the 2 groups given irradiated and nonirradiated milk

One criticism against this type of study is the choice of the control group. The control diet is described as being largely carbohydrate and deficient in protective factors. The only valid conclusion that can be drawn in that a deficient diet was partially but inadequately supplemented by the addition of 1 pint of milk per day. There is a distinct need

for well controlled nutritional studies on sufficiently large groups of children to permit statistical analysis. However, the control group should receive as nearly as possible a diet adequate in all but a single factor.

Dental Caries

Studies directed toward clarification of the etiologic factors involved in dental caries are being sponsored by the United States Public Health Service under the direction of L. M. Waugh. These studies are being conducted among a group of Eskimos which includes primitive natives, with little contact with white men. and less primitive natives in closer association with outside influences. Both the clinical and bacteriologic findings appear to indicate that the rather extensive dental caries which occurs among the less primitive Eskimos is the counterpart of the dental caries found among other peoples, with a single notable difference The evidence indicates that the dental carries among these Eskimos is largely a disease of recent origin. Its distribution is limited mainly to the younger natives, the older ones, even though they have lived in or near white settlements for many years, showed few indications of the disease. It may be significant that the types of dental carries observed among the natives, which are almost exclusively occlusal and proximal, are those generally commonest in all populations, which are particularly associated with young persons. If, as has been suggested, the varieties of dental caries more commonly associated with adultsparticularly caries of smooth surfaces of the teeth in the gingival and root areas have a separate etiologic basis, the problem of the cause of dental caries among these Eskimos is simplified by the virtual absence of such varieties.

T. Rosebury and M. Karshan²²³ made a study of the dietary habits of the Eskimo subjects. While it is not unlikely that dietary factors play an important part in the production of the caries noted, the data collected by these authors indicate no such correlation. They state that most of the dietary conditions commonly held to be responsible for dental caries or its absence cannot be correlated with

the incidence of dental caries at the 3 Eskimo settlements studied. These uncorrelated conditions included dietary carbohydrate in general, cereal and grain foods, dietary protein and fat, calcium and phosphorus and probably vitamin D and the potential reaction of the diet. These conditions either lack influence on, or play secondary rôles, in the causation of dental caries among these people.

PARASITIC DISEASES

By Waldo E. Nelson, M.D.

Pinworms

Cellophane swabs have been recommended for obtaining material from the anus for diagnosis of pinworm infection. L Reardon²²⁴ points out that the cellophane swabs contain artifacts which simulate the ova of pinworm. The artifacts have a definite hyaline outline, usually ovoid, sometimes rounded, enveloping a dark, amorphous mass hvaline outline of the artifacts which appears to be composed of several layers resembles the transparent layers of cells of the ova The central mass is irregular, brownish or greenish with usually a clear space between it and the hvaline outline. Variation in size is great but usually falls within the range of the pinworm egg, so that size and appearance constitute a potential source of error in diagnosis of oxyuriasis. The similarity of the artifacts and the pinworm ova are illustrated in Figs. 5 and 6

Giardiasis

The pathogenicity of Giardia lamblia (Lamblia intestinalis) has been questioned by some observers. However, most of them think it capable of causing disease in a certain percentage of those infested. According to the study of

P. Véghelyi,²²⁵ three-fourths of the children infested with *Giardia lamblia* have symptoms or significant complaints which

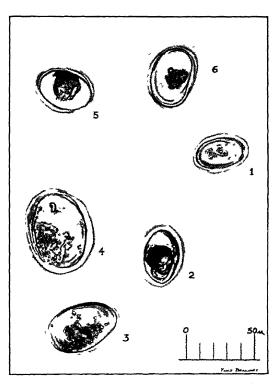


Fig 5—1 to 4 Artifacts in "Cellophane" previously used in swabbing 5 to 6 Artifacts in "Cellophane" not previously used in swabbing (Reardon Am J Trop Med)

can be related to the infestation. In the majority of instances, infestation is followed by an acute disease which may

		TABLE	7		
Effect	OF	TREATMENT	ON	29	CHILDREN

Findings	Before Treatment	After Treatment
29 children: Giardia present Anorexia Headache Dizziness Irregular bowel movement Abdominal pains	29 26 17 15 18 21 23	3 .; 3 1
19 anemic children: Average value of hemoglobin Average of erythrocyte counts	57% 3,009,000	89% 4,416,000
20 underdeveloped children. Average retardation Average monthly gain in weight over normal amount	38 months About 24 kg.	11 months

(Véghelyi Am J Dis Child)

become chronic, leading to anemia and abdominal complaints and impeding normal development.

Giardia lamblia has a vegetative and a cystic stage. Organisms in the vegetative

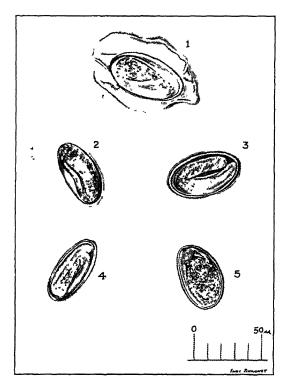


Fig. 6—1. Pinworm egg in n/10 NaOH. Outer shell distended 2 Pinworm egg in n/10 NaOH Outer shell dislodged 3 to 5 Pinworm eggs in tap water (Reardon: Am J. Trop Med)

form are easily found in the duodenal fluid. They seldom appear in the feces, except in case of severe diarrhea. Diagnosis can be made by finding the cysts which appear in the stools in practically every case.

While some of the infested children had no symptoms and others had symptoms of no significance, a high percentage of the infested children had gastroenteric complaints, anemia and madequate physical development. The symptoms consisted of anorexia, frequent headaches, and dizziness, irregular or frequent bowel movements, and pain in the abdomen, usually after meals. The children were anemic and thin They were underweight, but not under height. Muscular rigidity and pain on abdominal palpation were The pain was most frequently localized in the cecal or the hepatoduodenal regions but was not constant or localized to a circumscribed point. The liver was palpable in many instances.

Acetarsone (stovarsol) was used in treatment of this series of cases. The dosage was started at $\frac{2}{3}$ to $1\frac{1}{2}$ grains (0.04 to 0.10 Gm.) per day according to age and was increased to $3\frac{3}{4}$ to $7\frac{1}{2}$ grains (0.25 to 0.50 Gm.) per day. A

course of treatment lasted 3 weeks. In 29 of the 32 children treated, the parasites had disappeared by the end of the third week of treatment. The effect of the treatment on the 29 children who were apparently cured is shown in Table 7.

An instance in which giardiasis simulated celiac disease is reported by P Véghelyi.²²⁶ A boy, 25 months of age, had severely impaired physical development, with a large, protruding abdomen, hypotonic muscles, a dry skin, anemia, low calcium and phosphorous values in the blood and osteoporosis. He had large highly offensive, extremely fatty stools, 2 or 3 times a day Examination revealed serious diminution of the absorptive capacity of the intestines. The condition was attributed to an infestation with Giardia lamblia. After expulsion of the parasites, the child quickly put on weight; the intestinal absorption returned to normal, and the anemia and the symptoms of celiac disease disappeared. While the author does not infer that giardiasis is the sole cause of celiac disease, he does suggest that in children with the celiac syndrome, an examination for parasites should be made.

P. Véghelyi²²⁷ has demonstrated that absorption of fats is hindered in patients with infestation by Giardia lamblia. It is his opinion that the obstacle to absorption is of a mechanical nature and is caused by a layer of parasites adhering to the wall of the intestines. He has tested this assumption by studies of fat excretion before and after expulsion of the protozoa. In 8 of the patients who were successfully treated with arsenic and acridine compounds, the absorption of fats became normal after treatment. For example, in 3 patients whose fat excretion was over 70 per cent of fat intake before treatment, the fat excretion was only 5 to 7 per cent after completion of treatment.

POISONING IN CHILDREN

By Waldo E. Nelson, M D.

Atropine—Nine instances of poisoning from atropine are reported by H G Morton 228 In 2 of the cases, the only atropine administered was that instilled in the eyes for ophthalmoscopic exammation There appears to be a marked variation in the amounts of atropine which are tolerated by various children and adults. Poisoning has been reported in adults with doses of less than 160 grain (1 mg) and fatalities with $\frac{1}{30}$ gram (2 mg) of the drug In chilfatalities have been reported with doses as low as $\frac{1}{160}$ grain (04) mg) Four drops of a 1 per cent solution of atropine contain $\frac{1}{30}$ grain (2) mg) of the drug. The toxic symptoms are hot, dry, flushed skin, dilated pupils, nausea, diarrhea, delirium, staggering gait and coma Treatment should include administration of such parasympathetic drugs as pilocarpine, physostigmine, acetylcholine, and muscarine until the mouth is moist, copious lavage of the stomach, cerebral stimulants if coma is present, and catheterization of the bladder High temperatures should be controlled by alcohol sponges, and by the forcing of fluids.

Stramonium—Two cases of stramonium poisoning are reported by J. D. Hughes and J. A Clarke, Jr.²²⁹ Stramonium poisoning follows ingestion of any part of the Jimson weed, a plant

prevalent in this country and in all temperate and tropical zones. This weed is also known by such other names as Jamestown weed, thorn apple, stinkweed, devil's apple, and apple of Peru.

When the seeds or leaves are eaten, it may take hours for the symptoms to develop; but when a tea made from the seeds is drunk, as in the author's 2 cases, the onset may occur within minutes. Poisoning by the seeds usually causes a maniacal condition while ingestion of the leaves produces a comatose state degree of poisoning depends on the total quantity of the active principles of the weed absorbed, the potency of these principles, the promptness and effectiveness of the treatment and the sensitivity of the patient to the 3 alkaloids, atropine, scopolamine and hyoscyamine Progressively increasing thirst and disturbances of vision are usually early symptoms Other early symptoms which have been described are a sense of intoxication, euphoria, irritability, restlessness, and fear. On physical examination there is extreme dilatation of the pupils with no reaction to light or to accommodation. The skin is usually flushed, hot, and The surfaces of the mucous membrane are dry and hyperemic, unless collapse with evanosis is present. The neck may be stiff, and there may even be opisthotonos associated with convulsions. Tachycardia is a constant symptom Fever may or may not be present, temperatures as high as $105^{\circ} \, \mathrm{F}$ (40.5° C) have been recorded

Treatment to be effective must be prompt The stomach should be lavaged with water or 4 per cent tannic acid solution, which precipitates the alkaloids. Magnesium sulfate may then be administered through the stomach tube If difficulty is met in passing the tube, emetics should be given without delay

A drop of *croton oil* has been recommended for its purgative effect.

The authors administered soluble phenobarbital subcutaneously for its sedative effect. Morphine is contraindicated because of its tendency to cause cerebral congestion and because of its known synergistic action with atropine and scopolamine. Most patients recover in 1 or 2 days. However, the mydriasis may persist for a week or longer. An occasional death has been reported.

Chenopodium—A case of severe toxic encephalitis in a 2½-year-old child, resulting from the ingestion of 72 minims (46 cc) of oil of chenopodium over a period of 10 days is reported by T. L. Birnberg and C. L. Steinberg.²³⁰ In this case recovery followed forced perivascular (spinal) drainage and is of interest since cases of poisoning in which there are diffuse cerebral symptoms usually terminate fatally The authors' technic of forced perivascular drainage was as follows 04 per cent saline solution was given at the rate of 10 cc. per pound of body weight per hour. The child was placed on a Bradford frame, elevated on 12-inch blocks and a spinal needle was kept in situ in the fourth lumbar interspace throughout each treatment. From 900 to 1500 cc of the hypotonic saline solution were given at the rate of from 250 to 300 cc per hour, and the stylus of the spinal puncture needle which was left in situ was withdrawn every half hour

Lead—A case of lead encephalopathy in a breast-fed infant due to the use of lead nipple shields by the mother is reported by M Rapoport and A S Kenney.²³¹ The mother had worn the lead nipple shield constantly between nursings, the nipples being cleansed with boric acid solution before and after each feeding. The infant developed symptoms of encephalopathy at the age of 3½ months.

Improvement in a case of lead encephalopathy following treatment by adequate sedation together with a diet high in phosphorus including 30 cc. of a 10 per cent solution of disodium phosphate is reported by I. Kowaloff.²³² Evidence is presented to show that in this case the lead concentration of blood was determined by the lead-phosphorous product constant of the blood. This constant, expressed in the simplest form, is the product of the lead concentration in mg. per 100 cc. of whole blood and the inorganic phosphorous concentration in mg. per 100 cc of serum. In order to determine the chemical significance of this lead-phosphorous product constant, the author made the following assumptions (1) That the serum is a saturated solution of completely ionized dilead phosphate, PbHPO₄ (2) that the lead carried by the red blood corpuscles is in the solid phase of PbHPO₄, and (3) that the PbHPO₄ ions in the serum are in equilibrium with the solid PbHPO4 of the red cells The author also assumes that the proportion of lead per 100 cc of serum to lead per 100 cc. of whole blood is a constant. With this hypothesis, he was able to show that the solubility product constant of PbHPO₄, determines the lead and the phosphate concentration of the serum.

The author concludes that since there is good evidence that the principle of the solubility product constant is valid for the lead phosphate of the blood, a diet high in phosphorus (producing a high content of morganic phosphorus in the serum) would appear to be the most rational method of decreasing concentration of lead in the blood

Methyl Salicylate—A Eimas²³³ reports a case of methyl salicylate poisoning in an infant who swallowed 1 teaspoonful of oil of wintergreen. Vonuting was an early symptom and this was fol-

lowed by rapid breathing and drowsiness, and within a period of 12 hours the child had become quite stuporous. The child became cyanotic and after 24 hours had generalized convulsions. Death occurred 48 hours after the poison was taken. The temperature had risen to 105° F. (40.5° C.) and signs of pneumonia had appeared.

The symptoms of poisoning with methyl salicylate can be grouped under 3 headings, namely gastroenteric, respiratory, and central nervous system. Vomiting and diarrhea are frequent occurrences. The cerebral symptoms consist of marked irritability, increasing stupor, mental dullness, and generalized convulsions. Hyperpnea is a common and spectacular symptom. There is some question whether or not this is related to acidosis The similarity of the symptoms of methyl salicylate poisoning to those of diabetic coma have been noted frequently.

There is no specific therapy *Glucose* in physiologic saline solution should be given intravenously. Since there is frequently a lowering of the carbon dioxide combining power, this determination should be made at once and, if the CO₂ combining power is low, alkalis should be given at once either by mouth or intravenously

Phosphorus—A case of poisoning in an infant presumably resulting from phosphorus contained in an antirachitic preparation is reported by L. W. Sontag ²³⁴. The infant had received since the age of 1 month rather large doses of a cod-liver oil and malt preparation which contained ½ grain of pure phosphorus per fluid ounce (1 mg per 30 cc.) Sun baths were started at 6 weeks of age

Up to the age of 4 months the infant's gain in weight was rapid. From $4\frac{1}{2}$ to 6 months of age he gained no weight, and from 6 to 7 months of age there was only

a slow gain in weight. The infant became lethargic during that period. There was moderate anorexia but no vomiting or diarrhea. Although the infant appeared anemic, the blood count was within normal limits; however, the hemoglobin level was not stated. The calcium and phosphorous content of the serum was not determined. Roentgenograms of the long bones, taken at the age of 6 months, showed broad bars or bands in the ends of the long bones. At the age

of 7 months the mixture of cod-liver oil and phosphorus was discontinued, and a fortified cod-liver oil was substituted. In the first 2 weeks following this change, the child gained 11 ounces in weight The general condition was much improved; the skin turgor rapidly became normal; the lethargy disappeared; and motor development progressed normally. It was believed that the sun baths and the excessive vitamin D intake increased the toxicity of the phosphorus.

POLIOMYELITIS

By Robert A. Lyon, M.D.

Incidence—The prevalence of poliomy elitis between the years 1915 and 1937 has been reviewed by B. C. Hampton.²³⁵ Although the disease occurred in any season in parts of the United States, the peaks of incidence developed during the summer months from June to September More than 10,000 cases a year were reported in 4 different years, 1916, 1927, 1931 and 1935 Mortality rates have varied from 96 to 423 per cent with an average of 21.5 per cent, but some of these figures might not have been accurate because of unreported cases, especially during the early years of this period. Deaths per 100,000 population have ranged from 0.6 to 10.0.

The incidence of poliomyelitis in the United States during the year 1938 was the lowest of any year since 1916, according to the report of C C Dauer ²³⁶ The low morbidity rates were prevalent throughout all of the States with the highest rate in the District of Columbia (4.3 per 100,000 population). Alabama and Mississippi reported relatively high rates and Montana, Idaho, New Mexico, and Arizona had a slightly larger proportion of cases than the Country as a whole but

even their rates were quite low. In a few small areas of the South Atlantic States and in the Middle West, epidemics of considerable size had occurred.

Second Attacks—A second attack of poliomyelitis has been described by J. A. Toomey.²³⁷ The initial infection occurred when the patient was 3 years of age and the second one when he was 20 years of age. Eighteen patients with second attacks of this disease have been reported in the literature but the author raised the question whether or not these recurrences were true poliomyelitis. After an initial infection, the few remaining nerve fibers of an area may be especially liable to the influence of any toxic material so that many types of illness may produce a paralysis which is really a toxic neuronitis rather than a true poliomyelitis. With this possibility in mind, second attacks of poliomyelitis must be observed closely to determine whether an acute infection has merely aggravated an old poliomyelitis or is a true second attack of the disease.

Influence of Tonsillectomy — The relationship between the removal of tonsils and adenoids to the incidence of

poliomyelitis has been reviewed by R. C Elev and C. G. Flake.²³⁸ The disease was found to have occurred in a relatively large number of children within 30 days after the removal of their tonsils and adenoids, and the high incidence of bulbar types of the infection among these tonsillectomized patients was striking. Of a total of 131 patients with bulbar types of poliomyelitis, approximately 32 per cent had had their tonsils removed within 20 days prior to the onset of the disease It seemed likely that the tonsils might have been harboring the virus at the time of operation and the trauma to the tissues permitted entrance of the infection into the central nervous system. Attempts to reproduce this condition in animals failed.

Injury of the pharynx caused by the removal of tonsils and adenoids was also considered by A B Sabin²³⁹ to be a factor leading to poliomyelitis infections He was able to block off the nasal passages by the use of zinc sulfate spray in monkeys and then to produce polioniyelitis by the injection of the virus into tonsillar tissue. The instillation of virus into the nasopharynx in animals who had recently had their tonsils removed did not produce poliomyelitis but the injection of the virus into the tissues seemed to be the necessary factor causing the disease Tonsillar injection usually produced bulbar infections which developed rapidly with symptoms of a paralysis of the cranial nerves. Nasal sprays had protected the animals from invasion of the virus by way of the olfactory bulb, since this organ was found to be entirely normal at post-morten examination. The pathway of the virus to the brain must have been along the tracts of other peripheral nerve fibers. It seemed likely that poliomyelitis which has been observed frequently in patients who have had recent tonsillectomies probably resulted from the presence of the virus in the tonsils which was liberated by the trauma of the operation so that the infection could spread into the brain tissue. The author concluded that it would be unwise to perform this operation in patients during seasons in which poliomyelitis was prevalent in the community.

The influence of tonsillectomy on the occurrence of bulbar poliomyelitis has also been reviewed by M. Stillerman and A. E. Fischer ²⁴⁰ Among 10 patients at the Willard Parker Hospital in 1935 who had had their tonsils removed within a month preceding the onset of poliomyelitis, 6 developed bulbar or encephalitic forms of the disease. In the year 1937 there were 3 patients who had had their tonsils removed within a month preceding the illness and all had bulbar types of the disease. The first symptoms of poliomyelitis usually occurred in 10 to 21 days after the operation. The incidence of bulbar or encephalitic types of poliomyelitis was much greater in this small group of operated patients than in the total series of children who had the disease during the entire epidemic was thought probable that the virus gained entrance to the central nervous system by way of the broken mucous membrane of the pharvnx These authors also concluded that during the epidemics of poliomyelitis, tonsillectomy should not be performed

Etiology and Pathology—The fate of poliomyelitis virus instilled into the noses of monkeys has been studied by A B Sabin and P K Olitsky ²⁴¹ Shortly after the virus was placed in the noses of normal monkeys, it disappeared from the nasal mucosa and could not be detected in the olfactory bulbs during the first 48 hours. At the end of 72 hours, small amounts reappeared in these 2 localities and then gradually disappeared during the next 24 hours. In

immune convalescent animals, the virus disappeared from the nasal mucosa shortly after its instillation and did not reappear. It was concluded that the transmission of the disease in man by droplet nasal secretions would be very difficult unless much larger quantities of virus were transmitted than were employed in the above experiments, or unless human susceptibility was greater than that of experimental animals, or, finally, unless the virus was sometimes much more virulent.

J. A. Toomey²⁴² has been able to produce polomyelitis in monkeys by intravenous injections of the virus, after the olfactory nerve had been cut. Some of the animals, both in the operated and in the control series, resisted infection even though massive doses of the virus were administered.

This experiment would indicate that the virus reached the central nervous system by some other route than by its secretion into the nasal cavities after intravenous injection and resorption by the olfactory nerve.

The virus has been recovered from the intestinal tract as well as from the nose and throat secretions of patients and experimental animals by S D Kramer, B. Hoskwith and L. H. Grossman 243 Nasal washings and the stool or intestinal contents of 20 patients in various stages of poliomyelitis and from 7 monkeys at the height of the disease were examined Four strains of the virus were isolated from 3 patients, twice from nasal washings and twice from the feces. The virus was obtained on the fifth to ninth day of illness From 1 monkey, the virus was recovered from the upper intestinal tract It seemed probable that the chief route of infection was by way of the nasal or oral mucous membranes and probably the disease was spread by the contact of 1 individual with another. The fact that the virus can survive gastric digestion and occur in the feces would be strong evidence that greater precautions should be taken in the disposal of the feces of poliomyelitis patients to prevent the spread of the infection.

The pathological changes in the nervous system of monkeys infected intranasally with poliomyelitis virus have been reviewed by H. K. Faber.²⁴⁴ The pathway of the virus began with involvement of the olfactory bulb, progressed to the brain stem at about the level of the medulla and finally down the spinal cord until it localized there in certain areas, often more pronounced on 1 side than the other. The author was inclined to believe that this was the usual route taken by the virus in causing the infection in man and experimental animals.

Infection by way of the intestinal tract has not been proved definitely because all of the experiments of this type have required traumatic injury to produce an invasion of the virus The lesions in the brain stem usually followed the order described above but there was some variation in the speed with which this process occurred The nerve cells of the upper portion of the brain stem seemed to be fairly immune to the virus but there was a distinct susceptibility of the anterior horn cells of the lower spinal tract. The variation in susceptibility of the various cells and the possibility that the virus might be destroyed before it reaches the lower motor cells may account for the occurrence of abortive nonparalytic types of poliomyelitis and for the complete recovery noted in many patients

The invasion of the olfactory bulb seemed to be accompanied by a fever response by the patient and when the brain stem became involved symptoms of fever, vomiting, headache, general malaise often developed. The invasion of the posterior and lateral horns of the dorsal ganglia of the spinal cord usually

produced pain and tenderness and a positive Kernig sign. When the anterior horn cells became involved and destroyed, the weakness and flaccid paralysis occurred. As a rule, the cerebral spinal fluid contained no abnormal constituents until the latter part of the invasion of the brain stem and then the changes in the fluid continued as the virus progressed down the cord.

Variations in the antibody content of the blood serum of patients with poliomyelitis have been detected by J. F. Kessel, F. D. Stimpert and R. T. Fisk ²⁴⁵ Various strains of poliomyelitis virus were employed in the test. The results differed considerably, depending upon the type of virus used but as a rule the serum from patients who had nonparalytic types of infection had larger amounts of antibodies than the serum from paralytic patients Usually, the amount of neutralizing antibodies in the serum obtained from patients convalescent from poliomyelitis was greater than that present at the onset of the disease. This would indicate that antibodies developed throughout the course of the disease. However, a fairly large number of patients, more frequently adults than children, had slight or moderate amounts of neutralizing antibodies in their blood serum at the onset of the infection, which suggested that these individuals had had some previous experience with the disease, but that this type of immunity did not protect them from the infection The percentage of increase in the amount of neutralizing substances from the time of onset of the disease to the convalescent period was about equal in children and adults When the amounts of neutralizing antibodies found in individuals exposed in different years were compared, it was noted that at the end of a severe epidemic, convalescent patients had augmented amounts of neutralizing substances to virulent strains of the virus. Exposure to virulent strains of the virus, therefore, seemed to cause corresponding increases in antibody production.

Treatment—Sulfapyridine caused a drop in temperature and relief from pain in a patient with poliomyelitis treated by J. C. Wagner.²⁴⁶

No beneficial effects of sulfapyridine in the prevention of experimental poliomyelitis could be seen by J. A. Toomey and W. S. Takacs.²⁴⁷ Four monkeys received the drug in doses of 0.5 Gm. twice a day, beginning the second day after intracerebral inoculation with the virus. Four other monkeys served as controls The levels of sulfapyridine in the blood of the treated monkeys varied from 1 2 to 8.2 mg. per cent, and all of the animals developed the disease

The best treatment for all poliomyelitis patients with respiratory paralysis was artificial respiration by means of the Drinker respirator, according to the report of H. H. Hyland, W. J. Gardiner, F. C. Neal, W. A. Oille and O. M. Solandt, 248 Difficulties arising from spinal, bulbar or combined lesions seemed to require this type of artificial respiration. When the vital capacity of a patient of the author's series was reduced to 1500 cc or less he was placed in the respirator The main causes of death in such patients were depression of the cardiovascular and respiratory centers, or pneumonia. In order to avoid the latter disease, sterile technic and the wearing of masks by attendants was required and draughts or other irritating conditions were excluded as far as possible Care was taken to have trained attendants on duty at all times with equipment handy for keeping the trachea free from secre-The position of the patients was changed frequently and careful attention given to the prevention of urmary retention, constipation, and skin infections.

Of the 16 patients with respiratory paralysis, 10 had bulbar lesions. Seven of the entire group died. Four of the surviving group had bulbar involvement, but 3 of these will require prolonged treatment in the respirator. The length of time required for the patient's stay in this apparatus could be judged fairly accurately by tests of vital capacity but the rate at which the vital capacity improved differed widely in various patients Readings of 2000 cc. were usually obtained before the patient was taken out from the respirator.

Success wth the use of the Drinker respirator in cases of respiratory paralysis depends upon the type of patient selected. A. V Stoesser and W Sako²⁴⁹ reported successful results in 8 cases of poliomyelitis with involvement of the intercostal and phrenic nerves. Patients with respiratory difficulty which is bulbar in origin did poorly in the Drinker respirator because the instrument caused forcible aspiration of throat secretions into the lungs. Two patients with bulbar involvement and pharvingeal or laryingeal paralysis who were treated in this manner died after such treatment. Of a series of 13 patients treated with postural drainage, all but I survived. Good results may be expected with the respirator if the entire pharynx is not paralyzed.

Prevention — Persistent loss of the sense of smell or disturbances of taste have occurred in patients who have used nasal sprays of zinc sulfate for the prevention of poliomyelitis. A group of such patients has been collected by F. F. Tisdall, A. Brown and R. D. Defries.²⁵⁰ Thirty-six children between the ages of 3 and 10 years had suffered a loss of smell for a period of at least 2 months, and 52 others continued to have the loss of sensation when examined at the end of 6 months. The complaint was commoner among the older children. Eleven patients had a persistent disturbance of both taste or smell following a single nasal spray and 39 developed the complaint after 2 sprays. It was concluded that further studies should be made of the nature of the damage which is produced to the nerve endings by the zinc sulfate

A histological study of the effects of zinc sulfate on the olfactory nerves of rats has been made by C G Smith ²⁵¹ He examined the 3 types of cells present in the membranes of the nose of the rat, all of which were destroyed quickly by the application of a 1 per cent zinc sulfate solution. After a period of 12 days some of the supporting cells began regeneration but there was no evidence of regeneration of the sensory nerve cells

RESPIRATORY SYSTEM

By Waldo E Nelson, M D.

Upper Respiratory Infections

Otitis Media—Convincing data which indicate that reduction in the incidence of purulent otitis media in infants may be accomplished by conservative treatment are presented by H. Bakwin and H Jacobziner.²⁵² It is the authors' opinion that premature and unwarranted

myringotomy is one of the chief causes of purulent otitis media. They believe that incising an inflamed drum often leads to a purulent discharge in an ear in which, if there were no operative interference, the infection would subside spontaneously. They also suggest that frequent examinations of the ear, by trau-

matizing the drum and the canal and by exposing the nasopharynx of the infant to the expired air of the examiner, favor the development of purulent otitis media.

The results of their study lend no support to the view that delay in incising an ear drum is harmful to the child. When doubt exists, they believe it is preferable to wait. In acute intestinal intoxication, where a specific relationship to purulent otitis media has been suggested, the incidence of aural discharge has been reduced to one-third, by conservative treatment of the ear, with a fall rather than a rise in case fatality from the intestinal disease. The authors list the indications for myringotomy as complete obliteration of the landmarks, especially the short process, a bulging gray drum, together with fever, restlessness, and disturbed sleep When the pain seems intense, together with great restlessness and loss of sleep, the above criteria may be modified

Sinusitis—An intranasal method for treatment of acute sinusitis has been described by S. N. Parkinson ²⁵³ Ephedrine in Locke's solution is instilled into the nose with the child in the so-called lateral head-low position. The principle is to place the child's head in such a position that the solution will enter the sinal ostiums by gravity. The lateral head-low position is a modification of the head-low position is a modification of the head-low posture advocated by Proetz The patient lies on his side with his head bent downward, exactly sideways, using the shoulder as a fulcrum.

In treatment, preliminary shinkage is obtained by the use of ephedrine solution from an atomizer. This may require from 5 to 10 minutes. The patient is then placed in the lateral, head-low posture, and ephedrine in physiologic saline solution is instilled into both nasal chambers simultaneously. After from 3 to 5 minutes the child is placed face down to per-

mit the nasal content to escape from the nostrils. It is stated that none of the therapeutic fluid need reach the pharynx or mouth in this posture or during any part of the treatment.

Pneumonia

Etiology and Mortality — A comparison of the etiology, death rates, and bacteremic incidence in the more frequent primary pneumonias occurring in infants, children, and adults has been made by J. G. M Bullowa and M Gleich.²⁵⁴ This study was carried out over a period of 7 years. The data were based upon the 10 types of pneumococci most frequently found and the nonpneumococcic pneumonias were classified as "streptococcus," "streptococcus beta," "staphylococcus" and "bacillus friedlanderi." The pneumococci were types I, II, III, IV, V, VI, VII, VIII, XIV, XIX.

These 10 types of pneumococci represented 63 per cent of all the pneumococcic pneumonias in infants 788 per cent in children, and 745 in adults. The mortality for these 10 types among adults was 269 per cent, among infants 162 per cent, and among children, 41 per cent.

In the pneumococcic pneumonias, the blood was most frequently invaded in adults (23.5 per cent). The rate for infants was 6.7 per cent, for children, 4.1 per cent. In the positive blood culture cases, infants showed the highest death rate (83.3 per cent), adults, 74.1 per cent, and children, 25 per cent.

The 4 important classifications of non-pneumococcic pneumonias represented 66.7 per cent of all nonpneumococcic pneumonias in infants, 84.3 per cent in children, and 76.6 per cent in adults. In these cases the death rate was 29.8 per cent in adults, 21.2 per cent in infants, and 4.6 per cent in children. These fig-

ures parallel those of the pneumococcic pneumonias.

In the nonpneumococcic pneumomas, the blood was most frequently invaded in adults (16.1 per cent). In infants it was 4 per cent and in children, 17 per cent. In the positive blood culture cases, infants showed the highest death rate (100 per cent); adults, 95 per cent, and children, 75 per cent.

Staphylococcic Pneumonia — According to A Kanof, B. Kramer and M. Carnes,²⁵⁵ there are in general 2 types of staphylococcic pneumonia. In the primary cases, the history was chiefly that of an upper respiratory tract infection, with subsequent extension of the inflammatory process to the lungs. In the secondary cases, the history was that of a sepsis with the development of pneumonia as an additional and often terminal incident. In the primary cases, the physical findings were limited to the respiratory tract. In the secondary cases, the clinical picture was dominated by the symptoms referable to primary and suppurative foci other than the lungs Blood cultures were sterile, or at most there were only transient bacterial invasions in the patient with primary pneumonia, whereas in the secondary cases the blood stream invasion was heavy and persistent. The necropsy findings were almost entirely limited to the lungs in the primary cases, whereas in the secondary cases there was involvement not only in the lungs but throughout the body, and the pulmonary blood vessels showed widespread embolization The portal of entry in the primary cases could not be proved However, the authors believe it to be bronchogenic They suggest that the small bacterial invasion of short duration in the blood stream has the same relationship to primary staphylococcic pneumonia as the transitory early pneumococcemia has to pneumococcus pneumonia. It does not necessarily mean that the pneumonia is secondary to a sepsis. The possibility that staphylococcic pneumonia is a secondary infection, for example, following a virus disease, is considered.

The primary cases of staphylococcic pneumonia had certain similarities to pneumococcic pneumonia. Among the points of resemblance were the same incidence of positive blood cultures, the same distribution of cases in winter and early spring months, and the same relationship of upper respiratory infection and lung infection. There was often the same type of fastigial temperature commonly associated with pneumococcic infection, the onset was acute in both instances; and lobar involvement was common in primary staphylococcic pneumonia

The points of difference between primary staphylococcic pneumonia and primary pneumococcic pneumonia were The staphylococcic cases occurred predominantly below 1 year of age and the onset and course were more often fulminating in a previously healthy child Empyema occurred in more than three-fourths of the staphylococcic cases with pyopneumothorax in 2 cases The empyema fluid in about 20 per cent of the cases indicated there was destruction of tissue and bleeding into the pleural cavity. There was a greater tendency toward the occurrence of diarrhea and distention in the staphylococcic cases, and also a greater tendency toward renal involvement. Mortality in this series of cases of primary staphylococcic pneumonia was 65 per cent, overwhelmingly greater than in pneumococcic pneumonia

Virus Infection — Five cases of a hitherto undescribed virus infection of the lungs of infants, especially following measles and whooping cough, has been described and reported by E W. Goodpasture, S. H Auerbach, H. S. Swanson

and E. F. Cotter.²⁵⁶ The virus invasion usually appeared to be secondary and tended to pave the way for bacterial infection of the lungs. The presence of the virus was indicated by the occurrence of nuclear inclusions in epithelial cells of

fants. Experimental inoculation of infected lung tissues into animals has failed to establish the infection.

Giant Cell Pneumonia—The hypothesis that the giant cells of giant cell pneumonia represent metaplasia of alveolar

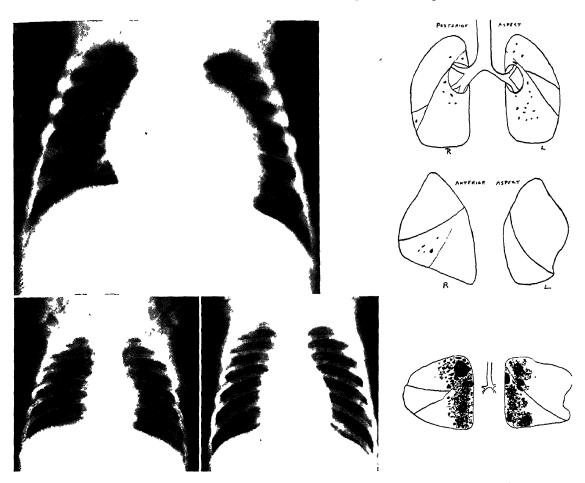


Fig 7—(Above)—Age 17 months Severe rickets The small scattered dense areas spreading in all directions from the right hilum are due to lipoid deposits in small amount. Shadows such as these are also caused by atelectasis accompanying rickets. Diagrams in this illustration were drawn from post-mortem specimens.

(Below)—Age 5 months Moderate involvement Roentgenographic changes confined mostly to the right side, in films exposed 5 weeks apart. Deposits of oil also present in the left lung at autopsy are hidden by the shadow of the heart in these anteroposterior roentgenograms. (Bromer and Wolman: Radiology.)

the trachea and bronchi and their mucous glands and of the alveolar epithelium Rapid necrosis of the affected cells occurred, resulting in ulceration of surfaces. The virus appeared to be different from that of herpes simplex and from the agent of the so-called inclusion disease of in-

epithelium due to vitamin A deficiency has been suggested by B Chown.²⁵⁷ The question is far from proved, since, for example, in some of the cases reported, the dietary histories did not reveal a deficiency of vitamin A. The question is raised whether infection can cause either

local or general depletion of vitamin A and result in metaplastic and hyperplastic changes of the epithelium of a single system. The question is an important

of giant cell pneumonia, there is an increased need for vitamin A. As Chown points out, proof or disproof must await experimental evidence.

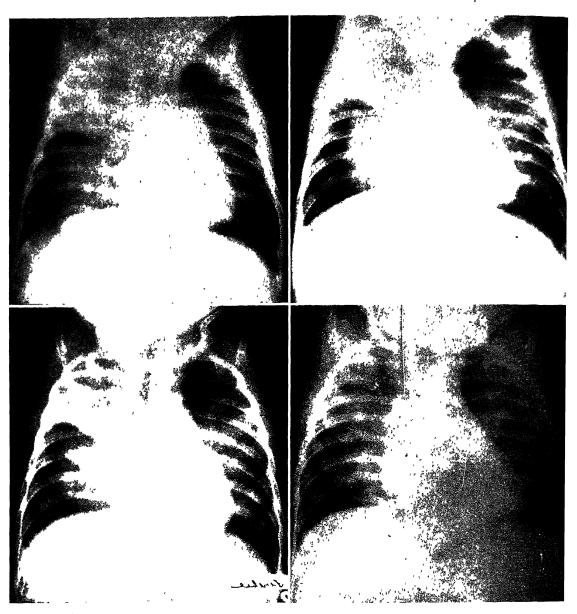


Fig 8—Severe involvement Clinical and roentgenographic diagnosis only. Time interval between first and fourth roentgenograms, 8½ months. The dense consolidation in the right upper lobe partially cleared, but the persistent densities demonstrate the chronicity of the process. (Bromer and Wolman: Radiology)

one, particularly in relation to what constitutes optimal vitamin A intake in health and in disease and whether in such conditions as measles and tuberculosis, both of which may be precursors

Lipoid Pneumonia—The roentgenographic appearance of lipoid pneumonia in infants and children has been described by R. S. Bromer and I. J. Wolman.²⁵⁸ The roentgenograms of the patients having only a mild involvement show an increase both in the degree of density and in extent of the hilar shadows. The linear markings of the lung fields are more exaggerated than normal. There may be scattered areas of increased density of very small size situated usually along the descending branches of the right bronchus. The heart shadow obscures the left hilar markings. In patients with moderate involvement, there is greater density of the perihilar shadows with widening in all directions. The dense shadow spreads more or less homogeneously in all directions from the hilum. In several of their cases, the left lung was entirely unaffected.

In the severe cases, the perihilar shadows spread well out toward the peripheries of the lung, although usually a clear zone is left between the dense shadow and the chest walls. As the child grows, this clear zone becomes wider unless the aspiration of oil has been maintained. The edges of the lesions are either sharply demarcated or feathery. The oily deposits may extend up to the pleura, in which case the dense area extends to the chest wall. Examples of their cases are illustrated in Figs. 7 and 8

Important studies concerning the potential dangers of intranasal medication and their possible association with lipoid pneumonia have been carried out by P. R Cannon and T E Walsh 259 Various types of nasal oils were instilled in small quantities into the nostrils of normal rabbits. The lungs were exammed microscopically from 24 to 48 hours and longer after the treatment. The authors found that the oil would go quickly and directly to the lungs, presumably because of the failure of the epiglottis to prevent their entrance into the trachea. The same mechanism operates in human beings. They found that the medicated nasal oils, even plain light mineral oils,

were definitely toxic to pulmonary tissues, causing edema and the characteristic picture of acute lipoid pneumonia. Usually, there was no secondary infection, but if living bacteria were added to the oils, as could occur if oils passed through an infected nasal passage, acute bronchitis, bronchial pneumonia, or granulomatous nodules would develop. They suggest that the general assumption that mineral oil is not particularly toxic to pulmonary tissues is probably due to the fact that its effects have not been observed within a short period of time after aspiration. While it is not as irritating immediately as many of the aspirated oils, it is nevertheless definitely toxic

In view of these findings, the authors performed similar experiments with the watery solutions of the commonly used nasal antiseptics in order to see whether these too would go directly to the lungs after intranasal inspiration and cause damage to pulmonary tissues. The socalled "mild" silver protein solutions, 5 and 10 per cent neosilvol and argyrol when placed in the nostrils of normal healthy rabbits went directly to the lungs as did the nasal oils and caused pulmonary edema, necrosis, hemorrhage, and focal bronchopneumonia These effects were more severe when the antiseptic solutions were put into the nostrils of rabbits with snuffles or were mixed with living bacteria isolated from the nostrils of rabbits with snuffles

The authors have also found that other materials used in intranasal therapy are potentially dangerous. Such astringent solutions as zinc sulfate, sodium aluminum sulfate, pieric acid, and tannic acid, which have been used with the object of blocking the olfactory nerves against entrance of the virus of poliomyelitis into the brain, when placed in the nostrils of rabbits in the concentra-

tions usually employed, go directly to the lungs in sufficient quantities to cause focal pulmonary edema, necrosis, and desquamative pneumonia. In addition to the pulmonary damage, there is also the local damage to nasal epithelium.

Not all materials placed in the nostrils, however, caused damage to the lungs. The authors put solutions of various nasal constructors, particularly, saline sothe upper respiratory passages, the simultaneous entrance of the chemical irritant and bacteria into the lungs may devitalize the pulmonary tissues, create areas of greater tissue vulnerability, and thus set the stage for the development of bronchopneumonia.

Treatment of Pneumonia—Oxygen Therapy—The open box method of administering oxygen is recommended by

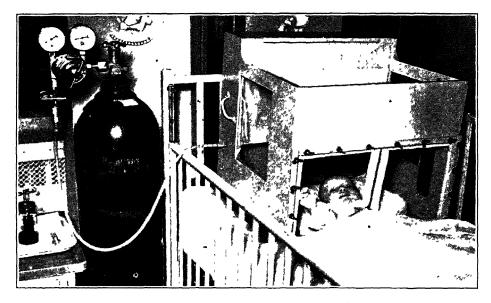


Fig 9—View of box in use showing a 4-month old infant within it The oxygen analyzer is seen at the left (Pachman J Pediat)

lutions of ephedrine and neosynephrine into the nostrils of normal rabbits and have observed no serious harm to the pulmonary tissues. Solutions of prontosil 1 per cent thymol, 1 per cent menthol, 10 per cent glycerin, and plain broth caused no harm.

It is obvious from these observations that extreme caution needs to be practiced in intranasal medication and that its widespread and uncontrolled use is to be condemned. The authors point out that since in the healthy, experimental animal, these medications may be toxic to pulmonary tissues, it appears quite probable that in humans and particularly in debilitated infants with purulent secretions in

D | Pachman 260 It has been adequately demonstrated that a satisfactory concentration of oxygen can be maintained With an inflow of 4 to 5 liters of oxygen per minute concentrations as high as 64 per cent have been maintained at the level of the patient's nose. The advantages claimed for this apparatus are (1) It is inexpensive to make and to operate, (2) it is simple to operate as no motors are needed; (3) the apparatus is portable and can be used in the home; (4) children can be fed without removal from the box; (5) the Phofilm windows allow for clear vision from within as well as from without; the children are not apprehensive; (6) examination and treatments can be carried out without removal of the patient from the box

The sides and back of the box are made of a light, nonporous wood. Clean, noninflammable x-ray films are used as transparent windows in the sides. Rubberized cloth forms the bottom of the box, but in front is replaced by a transparent rubber material, Pliofilm. The removable bottom and front is made in

Melted ice is drained from the container by means of rubber tubing into a collecting pail on the floor. The container also has a false bottom, and within it is a sponge to absorb condensed moisture. A hinged board acts as a cover to the ice cooler compartment. The oxygen inflow from a tank and regulator enters the side of the box directly on 1 side and the outlet for the drain is on the other.

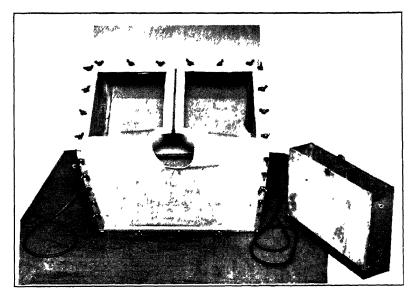


Fig 10—View of box showing the floor and the front piece The ice cooler is pictured at the right (Pachman, J. Pediat)

I piece and is fastened in place by strips of wood and thumb screws. In this manner the entire bottom is made airtight In the lower front is placed the aperture for admitting the head of an older child or the head, thorax, and arms of a small infant A 9-inch zipper allows this opening to be made larger. In the rear of the apparatus is the ice compartment which aids in maintaining a comfortable teniperature and humidity within the box Rubberized cloth acts as a baffle plate, separating the ice compartment from the front portion A metal ice container which has a tube in its base is suspended from a crossbar and is filled with ice about the size of refrigerator cubes.

The oxygen content within the box can be determined fairly accurately by means of a simple oxygen analyzer and should be analyzed every 4 hours. The authors use a modification of the method described by Henderson and Greenberg. Henderson and Greenberg. In measuring the sum of oxygen and carbon dioxide. The oxygen tent is illustrated in Figs. 9, 10, and 11

A buccal catheter for the administration of oxygen and oxygen mixtures has been devised by R Cohen ²⁶² The advantages claimed over nasal catheters and nasal tubes are that it does not obstruct the nasal passages and does not gag the patient. The instrument is constructed so that it lies adjacent to the buccal mucous membrane and lateral to the dentogingival area Only the inner aspect of the instrument, which is the side facing the oral cavity, permits the oxygen to escape. There is no interference with crying or with the administration of fluids

The construction of the apparatus is as follows: 2 brass tubes, $\frac{1}{16}$ inch in diam-

the oxygen tank. The distal end of the brass tubing is closed. Five perforations are drilled into the tubing of each pyriform wing on the side that faces the teeth. The chin rest has 2 hooklets on each side, 1¼ inches apart. These hooklets are raised portions of zinc or galvanized tin, ½ inch from each other. The chin base is moulded to fit the natural

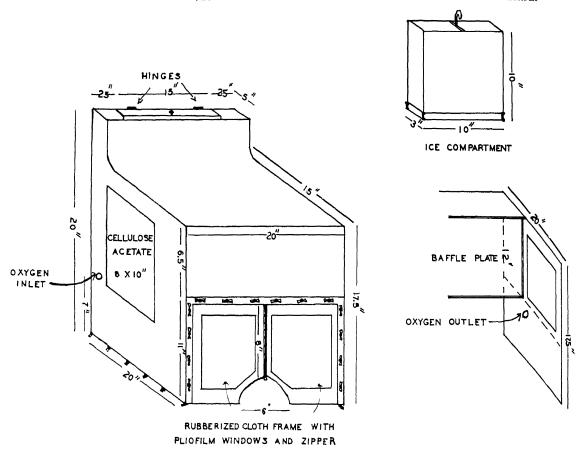


Fig 11-Dimensions of the various parts of the apparatus (Pachman J Pediat)

eter and 4¾ inches long are so shaped that they are pyriform at the end, that is, in the oral cavity. The portion of the tubing at the lower lip level is bent at an angle of about 110° with the chin base. One inch of tubing is allowed for resting on the chin base under 2 hooklets from which it may pivot. The final ⅓ inch of tubing is bent at right angles to the chin base. To this end of the brass tubing, rubber tubing is attached to lead to

curvature of the chin The 2 pieces of rubber tubing leading from the brass tubing to the glass Y-tube are held together by a metal ring. After the pyriform wings have been placed between the teeth and the buccal mucous membrane, this ring is adjusted over the rubber tubing in such a way that the pyriform wings are made to abduct and have more firmness against the cheek. The chin base is attached to the chin by adhesive tape.

The apparatus is illustrated in Fig. 12, A and B.

Serum Therapy—A 5-year study of the value of antipneumococcus serum in the treatment of pneumonia in 151 infants and children has been carried out by R. L. Nemir.²⁶³ The control group consisted of 253 untreated patients. Type I pneumococcus was the most predominant infecting organism in lobar pneu-

The author advises the use of serum for only severely ill patients whose cases are diagnosed early and for young infants, in whom the mortality rate is high. In the presence of a bacteremia, even though discovered late, sera are shown to be effective (in the author's experience I and XIV, certainly, and VII, V, II, probably). Indiscriminate utilization of serum for moderately or mildly ill chil-

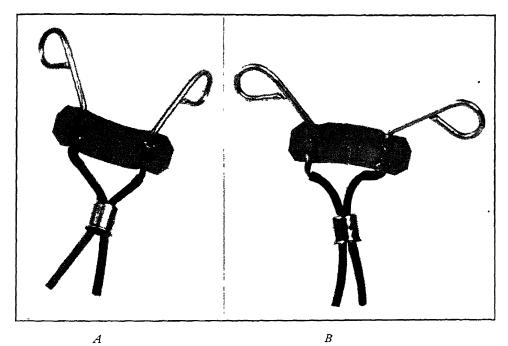


Fig 12—A Front view The ring about the tubing adjusts the abduction of the wings B Rear view This shows the perforations on the pyriform wings which face each other. (Cohen J. Pediat)

monia in patients more than 2 years of age, and Type XIV the most frequent pneumococcus in patients less than 2 years of age. The mortality rate for lobar pneumonia was low in each group and in the author's series the administration of serum showed no reduction. The incidence of empyema was reduced in patients with Types I, XIV, and V lobar pneumonia who received serum early in the disease. Late administration of serum in severely ill patients was valueless in preventing or reducing the development of empyema.

dren is inadvisable because of sensitization to horse serum. It is urged, however, that every patient with pneumonia receive a pneumococcus typing as early as the diagnosis is made, this may serve as a guide to the course and duration of the disease, incidence of complications, particularly empyema, and chances of fatality. The isolation of hemolytic streptococcus or pneumococcus. Type III may be an indication for the employment of sulfanilamide.

Sulfapyridine — Good results in the treatment of pneumococcic infections in

TABLE 8								
SULFAPYRIDINE	Dosages	FOR	Infants	AND	CHILDREN			

Age	1–3 mos	6 mos -1 yr.	2 yrs.	5 yrs.	12 yrs.
Dosage .	0 15 Gm	0 3 Gm	03 Gm.	0.6 Gm	09 Gm.
	every 4 hours	every 4 hours	every 3 hours	every 4 hours	every 4 hours

(Barnett, et al : J A M A.)

infants and children with sulfapyridine are reported by several groups. Among them are those of H. L. Barnett, A. F. Hartmann, A. M. Perley, and M. B. Ruhoff,264 and of A. T. Wilson, et al, A. H. Spreen, M. L. Cooper, F. E Stevenson, G E Cullen, and A. G. Mitchell.²⁶⁵ There was no selection of cases and no control group in Barnett's series Twenty-four children with pneumonia were treated, 3 of whom died. Two of these were infants with bronchopneumonia not proved of pneumococcic origin and 1 was an older child with lobar pneumonia complicated by severe larvingotracheitis, who died 12 hours after treatment was The dosages of sulfapyridine employed in this series are shown in Table 8

In Wilson's series, the effect of sulfapyridine was measured against a carefully selected control group. Seventy patients with pneumonia were observed, half of these received sulfapyridine lection of cases was made so that the 2 groups were essentially comparable in regard to age and duration and severity of pneumonia at the time of admission to the hospital. There were no fatalities in either group. The administration of sulfapyridine apparently shortened the course of the pneumonia by approximately 3 to 4 days. The series of cases was too small to allow evaluation of the effect of sulfapyridine in preventing complications of pneumonia. Two of the patients in the sulfapyridine group manifested a course apparently uninfluenced by the drug; 2 other patients had a relapse; and 1 had a series of relapses whenever the use of the drug was discontinued One patient in the control group had a relapse. On the basis of their observations, they suggest that a dosage which secures a level of free sulfapyridine in the blood of approximately 4 mg. per 100 cc. is therapeutically There were marked individual variations of the levels of sulfapyridine in the blood with the doses employed, namely, from 1 to 1½ grains (006 to 01 Gm) per pound of body weight each 24 hours. To be sure that an adequate dosage is being maintained, they advise daily examination of the blood The use of a photoelectric colorimeter makes it possible to perform determinations on 01 cc of capillary blood.

Empyema

L A Hochberg and B. Kramer²⁶⁶ have reviewed their experience with 300 cases of acute empyema of the chest in children In their experience, mortality from empyema was related to the severity of the secondary complications and not to the age of the patient. Complications, however, were associated with empyema more frequently in patients under 2 years of age than in those above that age The commonest complications encountered were pneumonia, pleurobronchial fistula, and lung abscess. The total mortality for those cases caused by the pneumococcus was 14 per cent, whereas the mortality for cases of complicated

empyema was 57 per cent and in cases of uncomplicated pneumococcic empyema was less than 1 per cent. In streptococcic empyema, the total mortality was 27 per cent, in cases of complicated empyema, 65 per cent, and in uncomplicated empyema, only 9 per cent. The total mortality for staphylococcic empyema was 37 per cent, for complicated empyema, 74 per cent, and in cases of

Closed intercostal drainage is said to have many advantages over the aspiration method in that it requires but 1 entrance into the pleural cavity and can be so arranged that it functions as a continuous drainage system. In the 88 cases of their series in which treatment was by intercostal drainage, there were 11 deaths and 20 cases in which this method was a failure. The most striking

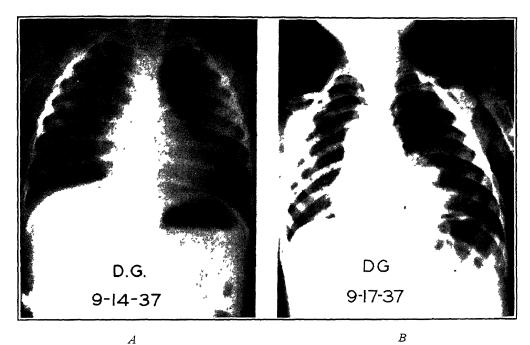


Fig 13—Case 1 A, small area of pneumonia, left lung B, 3 days later Emphysema of left lung causing shift of heart and mediastinum to the right (Shaw J Pediat)

uncomplicated empyema, only 10 per cent

The choice of the method of treatment appears to be of prime importance. It is their opinion that aspiration should be reserved for diagnosis and not for treatment. It is stated that repeated aspiration in the presence of a large pleural effusion is neither sound surgically nor innocuous. Particularly with staphylococcic empyema is there need for caution. Among the 76 patients treated by this method (aspiration) there were 38 deaths and 28 cases in which the treatment was unsuccessful.

and dramatic results of closed intercostal dramage were obtained in those cases in which the patient was acutely ill and in which there was cardiorespiratory embarrassment. If early surgical intervention is imperative during the acute pneumonic phase, regardless of whether the etiologic organism is the streptococcus, the pneumococcus, the staphylococcus, or a combination of several of these, closed intercostal dramage is the only method which can be employed with any degree of safety

Rib resection drainage appears to be the method of choice except in those

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cases in which the pus is thin or in which empyema is of very recent origin. Among the 151 patients treated by this method there were 8 deaths and 12 cases in which the patient failed to respond satisfactorily. Rib resection should be instituted after the acute pneumonic process has subsided and the pus has become thick. In cases of pneumococcic empyema, rib resection drainage may be insti-

often the end result of basal allergic bronchitis. If this is true, then bronchiectasis due to such a cause should be preventable if the basal allergic bronchitis is recognized and treated successfully. They state that basal allergic bronchitis can present all the clinical features of advanced bronchiectasis except bronchial dilatation as shown by the roentgenogram made after the injection of iodized

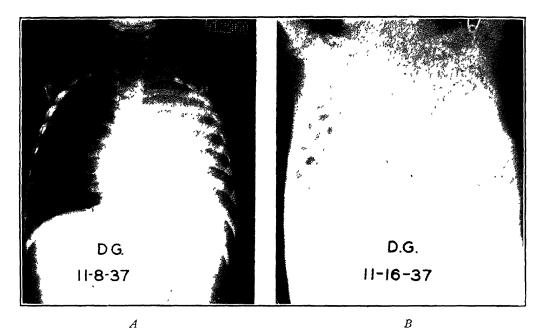


Fig 14—Case 1 A, 7 weeks later Obscuration of left hemothorax suggesting massive pleural fluid accumulation B, 1 day before death. Note great displacement of heart into right chest which autopsy showed was due to a greatly swollen lung. No pleural fluid was present. (Shaw. J. Pediat)

tuted as soon as the patient's condition begins to improve. In cases of staphylococcic empyenia, it should be performed as soon as intercostal drainage has proved inadequate.

Bronchiectasis

A new conception of the etiology of bronchiectasis has been suggested by S. H. Watson and C. S. Kibler ²⁶⁷. In their experience most patients with bronchiectasis have abnormal percentages of eosinophiles in their sputum or clinical manifestations of allergy. They believe that bronchiectasis is

oil The common sensitizations, in their experience, were to feathers, pollen, orris root, house dust and wool, although they have had a few cases in which foods were found to be causative factors

A Raia²⁶⁸ states that the *prognosis* of well established bronchiectasis is poor, although recent surgical advances offer a new hope in cases where no improvement can be expected from medical care. However, it is pointed out that the intelligent approach to the problem of bronchiectasis must be made through the recognition of those conditions which predispose to its

development Good results may be expected from the adequate care of the child with recurrent or chronic symptoms of the respiratory tract, even when early bronchial dilatation is present. Of even greater importance is the thorough treatment of each attack of pneumonia which is prolonged or which is preceded by measles or pertussis.

must be avoided and removal to warm climate is advisable when possible. The author states that freedom from recurrent infection for a year or more would aid complete healing of existing inflammatory processes more than any other single therapeutic measure.

Three instances of acute bronchiectatic abscesses simulating empyema are re-

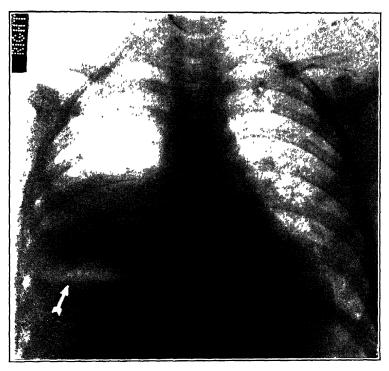


Fig 15—Case 1 Chest roentgenogram showing gas and fluid level beneath right leaf of diaphragm. This was noted 8 months after a diagnosis of appendicitis. At this time, patient was sent to hospital because of a diagnosis of pulmonary disease. (Anspach: J. Pediat.)

Such treatment should include the continuance of rest in bed, not only until the fever has subsided but until the physical signs and roentgenograms have completely cleared. Proper pulmonary drainage should be carried out by posture and, if necessary, by bronchoscopic treatment. Foci of infection in the sinuses and tonsils must be eradicated. General hygienic measures are of the utmost importance. A properly balanced diet with a high vitamin content is essential. Exposure to infection

ported by R R Shaw ²⁶⁹ The 3 cases represented severe bronchial infection superimposed on obstructive emphysema. The obstruction in the bronchus was presumably formed by thick secretions and swollen bronchial mucosa. It was assumed that the bronchial lumina were open during inspiration but closed during expiration, resulting in distention under considerable pressure beyond the obstructed bronchus, with consequent emphysema of the alveoli and the terminal bronchi. As the block becomes



Fig 16a—Case 3 Shadow at right base with fading horizontal upper border due to transphrenic infection. No gas and fluid level beneath diaphragm. (Anspach. J. Pediat.)

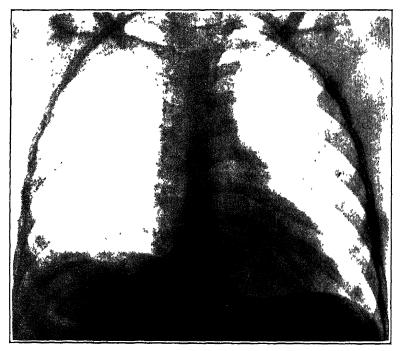


Fig 16b—Case 3 Eleven days after drainage of the abscess which followed preliminary marsupialization (Anspach J Pediat)

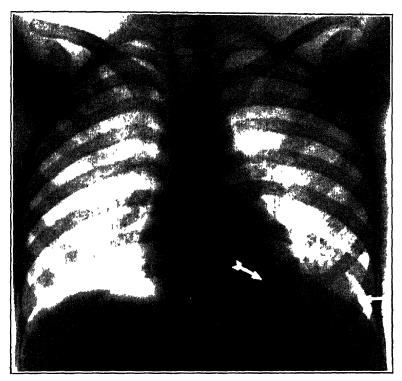


Fig 17a—Case 7 Density with convex outline left base following a local peritonitis (Anspach. J. Pediat)

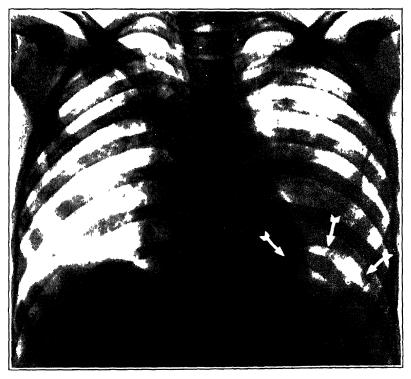


Fig 17b—Case 7 The pleural pocket has communicated with a bronchus and exchanged fluid for air. Here an adhesive diaphragmatic pleuritis has prevented separation of the pleura for more than a short distance. (Anspach. J. Pediat.)

more complete, and the secretions become dammed up, a severe bronchial infection results. This swelling causes mediastinal shift toward the normal side and the roentgenogram reveals a marked density in the involved hemothorax. This is apt to lead to the erroneous diagnosis of empyema. The mistake is apt to be made of performing a thoracotomy with rib resection. When the correct diagnosis of acute bronchiectatic abscess has been established, treatment should be directed toward improving bronchial drainage. This can be done by bronchoscopic aspiration or by intrabronchial suction with a soft rubber catheter introduced through the nose. One of the author's cases is illustrated in Figs 13 and 14.

Subphrenic Abscess

In reporting 10 cases of subphrenic abscess in children, W E. Anspach²⁷⁰ stresses the importance of the study of serial roentgenograms made early and during the course of the disease. The presence of a diaphragmatic pleurisy which arises in the course of a vague or definite abdominal complaint should arouse suspicion that a transphrenic infection may be present. Fixation of the diaphragm is the earliest roentgenographic sign, the evidence of diaphragmatic pleurisy next, then the signs of an accumulation of fluid which tends to

remain small in amount and later, even in neglected cases with extensive empyema, and the evidence of an almost normal contact of the visceral and the diaphragmatic pleurae (in overexposed films). The roentgenographic signs, which are almost pathognomonic of this disease, are the shadows of "gas and fluid level" beneath the right leaf of the diaphragm. However, these latter signs were present in only one-fourth of the author's group.

The roentgenographic signs of pneumonitis and collapse of the lower lobe are occasionally associated findings as the infection invades or surrounds the lung tissue. A local basal pneumothorax is prone to follow a bronchial fistula, with or without spontaneous healing A rest cavity is more common than in primary pulmonary disease The majority of cases follows appendicitis Small perforations in other viscera are thought to account for most left-sided cases. These appear to have a greater tendency to heal spontaneously than right-sided cases. Waiting for definite roentgenographic signs of loculation before establishing drainage appears to be judicious treat-Spontaneous recovery without drainage occurred in one-third of the cases reported Figs 15, 16, and 17 illustrate some of the findings of the author's series

SCARLET FEVER

By ROBERT A LYON, M.D.

General Considerations—The characteristics of scarlet fever in infants less than 2 years of age have been surveyed recently by A Stroe, H. Lazaresco-Bacaloglu and I. Schwartz.²⁷¹ In comparing the course of the disease in 5248

patients over 2 years of age with that of 534 under 2 years of age, they found that the younger infants suffered more frequently from severe types of scarlet fever; complications were more than twice as common; and the mortality rates

TABLE 9

RESULTS OF CULTURES OF MATERIAL FROM THE NOSES AND THROATS OF PATIENTS

ABOUT TO BE ADMITTED TO THE HOSPITAL

		1934			1935			1936		
Month	Total No of Patients	No. Pos.	Per- centage Pos.	Total No. of Patients	No. Pos.	Per- centage Pos	Total No of Patients	No. Pos.	Per- centage Pos.	
Tanuary	. 56	10	17.9	102	17	16.7	85	19	22,4	
February	83	20	24.1	114	25	21.9	59	17	28.8	
March.	156	40	25.6	99	30	30.3	87	16	184	
April	229	57	24.9	119	33	27.7				
May	263	68	25.9	141	33	23.4			1	
June	221	40	18.1	145	38	26.2				
July	267	45	169	130	16	12.3				
August	197	25	12 7	146	23	15.7				
September	236	26	11.0	127	17	13.4				
October	288	52	180	120	18	15.0				
November	268	47	175	120	15	12 5		١.		
December	179	31	173	114	19	16 7				
Total.	2,443	461	18.9	1,477	284	19.2	231	52	22 5	

Total number with cultures, 4,151. Positive cultures, 797 or 19.2%. (Peacock, Bigler and Werner: Am J. Dis. Child)

were higher The scarlatinal rash in the young infants was frequently atypical with a predominance of the flush and erythema but less papulation of the skin. The duration of the rash was frequently shorter and evidence of desquamation was often absent or consisted only of a fine powder. On the other hand, infants of this age group suffered greatly from severe throat infections and toxic manifestations of the disease.

The throat cultures of a large number of well individuals and of patients suffering from diseases other than scarlet fever were observed over a period of years by S Peacock, J. A. Bigler and M. Werner ²⁷² They found the hemolytic streptococcus more frequently in the children and personnel of a children's hospital than in those of a general hospital. On admission, the children were less apt to have positive cultures than after they had been institutionalized for several days. When cultures were taken from patients and personnel day after day, the incidence of hemolytic strepto-

cocci was about the same at one time as at another in the entire group but the individuals who had positive cultures varied so that about one-half of the number who had the organisms in their throats at one time did not have them at a later date. Cultures were positive less frequently and remained positive for shorter periods of time in children than in adults or in the personnel of the children's hospital who had been working for several months or years in the institution Nurses who were taking care of contagious hospital units had positive cultures more frequently than nurses on general duty.

The number of children with the hemolytic streptococci in their nose and throat secretions varied from season to season but the total incidence rates were about the same from year to year.

Positive throat cultures alone were obtained from 14.5 per cent of the children on admission to hospitals, positive nose cultures in 1.5 per cent, and positive nose and throat cultures combined in

TABLE 10
CHANGES IN DICK REACTION WITHIN 1 YEAR

Age	Total No of	No of Positive Reactors to	Positive Second Test		No. of Negative	Results of Second Test	
8*	Patients	First Test	Positive	Negative	Reactors to First Test	Positive	Negative
Under 6 mo 6-12 mo 12-18 mo 18 mo -2 yr 2- 3 yr 3- 4 yr. 4- 5 yr 5- 6 yr 6- 7 yr 7- 8 yr. 8- 9 yr. 9-10 yr 10-13 yr	69 55 38 75 70 74 83 73 82 59 59 61 60	15 39 29 53 60 65 69 58 57 50 41 37	12 30 28 45 55 55 60 50 53 45 34 34 30	3 9 1 8 5 10 9 8 4 5 7 3	54 16 9 22 10 9 14 16 25 9 18 24 23	27 3 1 2 3 2 1 1	27 13 9 21 8 9 11 14 24 8 18 24 22
Totals	859	610 71%	531 62%	79	249 29%	41	208 24%
Totals for all over 1 yr of age	735	556 76%	489 67%	67	179 24%	11	168 23%

(Peacock, Bigler and Werner Am J Dis Child)

about 3 per cent. Children with tonsils and adenoids had the hemolytic streptococci a little more frequently than others, but the incidence of positive cultures did not seem to be related to occurrence of respiratory infections of the children or their parents, the size of their families, or the age of the patients, except that children gave positive results more frequently than adults and children under 5 years of age were more frequently positive than older children.

Reactions to the *Dick test* were found to be changeable during the first year of life. Negative tests were more frequent in children who had had their tonsils removed than in unoperated patients and were more frequent in children of larger families than those of smaller families. In groups of children retested at the end of 1 year, reactions changed from positive to negative in 6 per cent more of the children who had had hemolytic streptococci in their nose and throat secretions

than in the negative group. Changes of the Dick reaction from negative to positive occurred in 1 per cent of the children over 2 years of age Positive reactions were detected in 13 to 23 per cent of groups of children who had had scarlet fever previously. In a survey of the incidence of scarlet fever among hospital patients, it was found that sporadic cases occurred infrequently in children's hospitals, and exposure could usually be traced to carriers of the hemolytic streptococci among the personnel or other patients Since the carrier rate is apt to be high in hospitals of this type and the number of children with positive Dick reactions is relatively great, the only way to prevent the occurrence of sporadic cases of scarlet fever seemed to be the requirement of negative Dick reactions in all of the children and personnel.

A study of the types of hemolytic streptococci in scarlet fever patients and in throats of well children has been con-

TABLE 11

Frequency of Scarlet Fever, Positive Dick Reactions and Positive Cultures in Various

Age Groups for 1934 and 1935

Age, Yr	Scarlet	Fever	Positive Dick	Positive Cultures,	
	No of Cases	Percentage	Reaction, Percentage*	Percentage*	
Under 1. 1 2. 3. 4. 5 6 7 7 8 9 10 11 12. 13–16 17–20. 21–30 31–45 Over 45	80 361 1,100 1,515 1,868 2,293 3,264 2,961 2,400 1,790 1,507 1,128 917 1,715 575 1,232 661 61 6**	0 3 1 4 4.3 6 0 7.3 9.0 12 9 11 6 9 5 7 0 5 9 4 4 3 6 6 7 2 3 4 8 2 6 0 2	34 71 75 69 61 54 48 41 41 32 34 27 28	11.2 14.5 20.9 16.7 24.4 23.5 24.7 26.3 19.0 23.8 32.4 20.1	
Total	25,442				

^{*}Results of culture and of Dick tests for 3300 children about to be admitted to the Children's Memorial Hospital

ducted by J H Bailey 273 A close relationship existed between the types of hemolytic streptococci found in scarlet fever patients and in the throats of grammar school children Over 90 per cent of the strains of streptococci isolated from children were capable of producing toxins of the scarlet fever type. The toxinproducing streptococci were found as frequently in the pupils of schools where scarlet fever was not epidemic as in those in which the disease occurred frequently The type of streptococcus isolated from scarlet fever patients at the beginning of the disease changed in character in at least 50 per cent of uncomplicated cases before the patients left the hospital There seemed to be no relationship between the incidence of complications and the change of type of streptococcus

Variations of immunity to scarlet fever of people living under different climatic

conditions have been studied by H. Plummer.²⁷⁴ The streptococcal antitoxin levels in the patients' blood sera were measured by cutaneous tests in rabbits The degree of immunity of individuals living in Canada was compared with that of natives of certain tropical areas A larger proportion of the tropical group had antitoxin levels adequate for immunity and the general level of the antitoxin titers was higher than in the case of the inhabitants of the temperate zone would seem that subclinical infections with the hemolytic streptococci had occurred earlier and more frequently in the tropical inhabitants than in those of the temperate zone Measurements of serum antitoxin levels of mothers were shown to be lower as a rule than those of the cord blood of their infants.

Inclusion bodies have been found in association with scarlet fever by J Broad-

^{**}Incomplete information (Peacock, Bigler, and Werner Am. J Dis Child)

hurst, G. Cameron, M. E. Maclean and V. Saurino.²⁷⁵ They have raised the question whether or not a virus might play some part in the etiology of this disease. The inclusion bodies were found in the cells lining the nose, tongue, and throat and in the mononuclear cells of the blood. These bodies could be produced in tissue cultures and in the cells of experimental animals inoculated with the blood serum of scarlet fever patients. In no instances were streptococci detected in these specimens of blood, and the sera from patients not having scarlet fever did not stimulate the production of inclusion bodies in animals

Complications—Some of the factors which influence the incidence and course of otitis media in scarlet fever have been reviewed by C. Wesselhoeft 276 In several very large series of scarlet fever patients reported by various investigators and in the author's own series of more than 9000 patients, the incidence of otitis media remained almost constant at about 12 per cent The incidence of the complication was much higher in the winter months than in the summer months irrespective of the times at which the peaks of scarlet fever morbidity occurred. Otitis media developed with the greatest frequency in children 2 years of age and the ratio decreased with advancing age age distribution, the incidence of this complication followed closely that mortality.

When other infections, such as diphtheria or measles accompanied scarlet fever, otitis media developed more frequently than in cases of scarlet fever alone. The presence or absence of tonsils did not affect the incidence of otitis media in the series observed by the author, although it has been reported elsewhere that scarlet fever occurs less frequently in patients who have had tonsillectomies. Paracentesis of the ear-

drum did not seem to reduce the incidence of mastoiditis and it was difficult to prove that the children whose drums ruptured spontaneously had any more severe complications than those whose eardrums were incised. The important factor in the treatment of otitis media seemed to be the early recognition of mastoiditis and immediate operation. The early administration of scarlet fever antitoxin seemed effective in reducing the incidence of otitis media. Sulfanilamide therapy has also seemed to have a beneficial effect upon the reduction of the occurrence of otitis media but further investigation of this question will be necessary before conclusions can be drawn.

The cardiac lesions of scarlet fever have been reviewed by P. Kiss and O. Malaguzzi-Valeri ²⁷⁷ Evidence of this type of carditis consisted of an unstable pulse, a soft first heart sound, sometimes cardiac dilatation, an arrhythmia, and often a soft systolic murmur or one of a harsher quality along the left sternal border. The cause of the heart condition is not known but it has been assumed that the scarlet fever toxin produces some temporary damage of the cardiac mus-In a study of 15 children with scarlet fever carditis, the authors were unable to explain the occurrence of the heart trouble on any other factors, such as weight change or anemia of the patient

Heart block occurred as a complication of scarlet fever in a patient observed by M. Bernstein ²⁷⁸ On the eighteenth day of a scarlet fever infection, the patient, who was 18 years of age and had not had any previous heart trouble, developed a slow cardiac rate of 50 to 60 per minute From that time onward he had symptoms of fatigue, dizziness, dyspnea, and severe precordial pain. About 1 year later, the first attack of unconsciousness occurred Electrocardiograms revealed a dissociation between the auricles and ventricles

and it seemed likely that the scarlet fever had been the etiologic agent. Such cases emphasize the importance of searching for cardiac symptoms in patients with scarlet fever. As a rule, the heart, if involved at all, will show evidence of damage during the second to fourth week of the disease.

Treatment—Comparisons between the therapeutic value of convalescent serum and that of scarlet fever antitoxin, made by F. H Top and D. C Young,279 indicated that they were equally effective. Alternate patients with scarlet fever received the respective sera and the average duration of their fever, the number and severity of their complications and length of stay in the hospital were approximately the same in each series. Further comparisons of the same factors in 3 groups, 1 receiving convalescent serum, another, scarlet fever antitoxin and the third a horse serum not containing scarlet fever antitoxin, showed that the 2 specific sera were much more beneficial than the nonspecific one however, there was no significant difference in the results obtained with convalescent serum and with specific antitoxin

Favorable results with the use of **sul**fanilamide in the treatment of scarlet fever have been reported by W Sako, P F Dwan and E S Platou 280 A group of 100 patients were treated with an initial dose of 3/4 grain (0.05 Gm.) of sulfanilamide per pound of body weight and ½ grain (0.03 Gm) per pound for each 24-hour period results occurred when the drug was continued throughout convalescence A control group of 100 children received no specific treatment Complications occurred in 8 per cent of the series treated with sulfamilamide and in 41 per cent of the control series. No differences in the rate of recovery from the toxic symptoms of the illness were noted in the 2 groups Since convalescent serum and commercial antitoxin act in combating toxemia primarily, the authors suggested that a combination of the sulfanilamide and convalescent serum would be the best method of treating both the toxemia and the streptococcus infection of scarlet fever.

Prontosil administered to scarlet fever patients gave good results in the series observed by J Ström.²⁸¹ The drug was administered to alternate patients throughout the period of 1 year. A series of 122 children received the therapy and an equal number served as a control group. There were 22 in each group who also received antiscarlet fever serum. The patients treated with prontosil had shorter periods of fever, only one-third as many complications and their sedimentation rates returned to normal more rapidly than the control group. The drug seemed to have very little effect on the toxic manifestations of the disease but the recurrences of infection were less frequent in the treated than in the control group and the complications of intercurrent infections were also less common in those receiving the drug Mild complications from the treatment occurred in 5 patients and were limited to skin rashes, fever, stomatitis, and glossitis.

The complications of scarlet fever were noted. Complications of the disease either pooled convalescent serum or sulfanilamide in the experience of P. Hamilton and Y Togasaki. The pooled serum was given intravenously in a single dose of 40 to 100 cc, depending upon the age of the patient. Sulfanilamide was given by mouth in quantities of 15 grains (1 Gm) per 20 pounds (9 kg.) of body weight over a 24-hour period. This dosage was continued for 3 days, reduced in amount for another 3 days,

and further reduced to one-third of its original quantity for the third of 3 days. No reactions to either kind of treatment were noted Complications of the disease developed in only 14 per cent of those treated with serum and in 10 per cent of those treated with sulfanılamıde of these rates were considerably below the average incidence of complications of scarlet fever (33 per cent) which had occurred in patients during a 5-year period when no specific therapy was employed The mortality rates declined from 2 per cent or more in untreated patients to 05 per cent in the groups receiving specific therapy The convalescent serum gave the most immediate results in respect to comfort and relief from symptoms and thereby shortened the acute stages of the disease The sulfanilamide caused no immediate response and the course of the acute stage of the disease seemed to be about the same as in untreated patients, but the drug had its most marked effect on the prevention of complications

Immunization - The results of unmuization of a large number of patients against scarlet fever have been reported by E. R. Krumbiegel ²⁸³. A total number of 6500 individuals received 3, 4, or 5 mjections of the scarlet lever toxin Of a group of 3914 susceptible persons who received 5 doses, all but about 7 per cent became Dick negative. During the subsequent years of observation, 0.88 per cent of this group contracted scarlet fever while more than 12 per cent of a series of persons who were not immunized had the disease. The differences between the incidence rates of the 2 groups diminished as the time went on, which might be explained in part by the fact that many of the unimmunized, during a period of 2 or 3 years, developed some immunity to the disease from subclinical attacks and, therefore, did not contract typical scarlet fever in as high percentages as at younger ages. Immunity disappeared much more rapidly in the individuals who received only 1 or 2 injections of the toxin than in those who received 3 doses or more.

Individuals who had had clinical scarlet fever were retested with the Dick test annually for 3 years after recovering from the disease In the first year, about 13 per cent had positive reactions: 3 years after the disease, about 19 per cent had positive reactions. Recurrences of the disease were reported in 68 of the 5965 patients with scarlet fever This incidence of second attacks was only slightly greater than the attack rate in negative Dick reactors and in the positive Dick reactors who had received complete courses of immunization. It seemed unnecessary, therefore, to test and to immunize patients who had a positive history of scarlet fever in the past

Attention was called to some of the discrepancies of the Dick test which might arise from technical errors, from nonspecific illnesses which might alter the Dick reactions temporarily, and from the variations of the Dick toxin prepared by different manufacturers. Some investigators have also demonstrated differences in the reactions produced by endotoxins and exotoxins of the scarlet fever streptococcus and further investigation of these fractions might be valuable.

The administration of the Dick toxin for immunization against scarlet fever has seemed to stimulate the development of antitoxin but not any streptococcal antibodies in the blood of the patients Experiments of M. M. Strumia²⁸⁴ have indicated that antifibrinolysins, antistreptolysins, and the agglutinins in 36 patients were not influenced by inoculations with the Dick toxin. In some of

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the patients, changes in the amounts of antibodies took place during the periods of observation and treatment but they

were not any more marked than a group of normal individuals who had received no treatment.

SMALLPOX

By Robert A Lyon, M.D.

A nonspecific illness developing in 7 vaccinated persons who had been exposed to a fatal case of smallpox has been described by E. T. Conybeare 285 The symptoms consisted of fever, headache, backache, severe perspiration and generalized muscle tenderness Revaccination of the group produced accelerated reactions. In 2 instances, eruptions occurred which may have been abortive forms of smallpox or vaccinia. The possibility of atypical or mild forms of smallpox occurring in individuals with partial immunity was thought to be of epidemiological importance.

Complications---Vaccinal encephalitis occurring in a child 14 weeks of age was treated with convalescent serum by E. Sakoschansky and H. J. Trenchard ²⁸⁶ The symptoms of the encephalitis developed about 10 days after the vaccination had been performed. Neck rigidity, fever, weakness of the right side of the face, the abductor muscles of the right eve and later a weakness of the left arm were prominent symptoms. The cerebrospinal fluid contained 60 lymphocytes, increased amounts of globulin and the gold curve showed reduction in the middle zones Ten cubic centimeters of whole blood obtained from an adult vaccinated 7 vears previously were given intramuscularly. Later the child received an additional 12.5 cc of serum obtained from an individual who had been vaccinated only 4 weeks previously with lymph from the same batch as that used in the patient The child recovered completely

Treatment—Sulfanilamide gave favorable results in patients with smallpox treated by W. O McCammon.²⁸⁷ In a group of 7 adults with the disease, 4 received sulfanilamide during the invasion period of the disease and 3 were given symptomatic treatment only One of the patients had had a successful vaccination 40 years previously but the others had never been vaccinated early symptoms of the infection were not modified by the sulfanilamide, but the eruption was much milder and the papules did not usually reach a purulent stage The macules which appeared on the skin were somewhat tender but disappeared within a week's time sulfamilamide shortened the course of the disease by about a week

Vaccination—Smallpox vaccine cultivated on artificial media may be employed safely as an intradermal vaccination T M Rivers, S M Ward and R D Baird²⁸⁸ have tested its efficacy in a group of 331 children. Most of these patients were vaccinated intradermally at the age of 6 to 12 months and all had "takes" consisting of papules and erythema but no vesicles or residual scars. When retested with the usual dermal method, employing calf lymph virus 1 month to over 3 years later, 25 per cent had minume takes and 75 had accelerated It seemed necessary, therereactions fore, to revaccinate all patients about 6 months after the intradermal vaccination with culture virus in order to obtain complete immunity. Such a procedure of double vaccination would reduce to a minimum the systemic reactions and the disfiguring scars to which many patients have objected.

Accidental vaccination of the nose occurred in a patient observed by S. G. Bedford and F. F. Hellier ²⁸⁹ A woman, 31 years of age, who had never been vac-

cinated, was exposed to the successful "take" of her child. Five days later a fissure at the corner of the left nostril became infected and a large area of vaccinia developed over the entire end of the nose with edema of the surrounding tissues and swelling of the cervical lymph nodes. The lesion followed a typical course and left some permanent scarring.

SYPHILIS IN CHILDREN

By ROBERT A. LYON, M D.

Acquired Syphilis

Acquired syphilis in children under 10 years of age is comparatively rare The clinical and epidemiological features of this form of the disease in 125 children observed in various large clinics throughout the country have been reviewed by F. R. Smith, Jr 290. The relative incidence of the infection was difficult to determine but in one clinic, the ratio of children with acquired syphilis to those with congenital syphilis was 1:23 and the acquired disease in children under 10 years of age constituted I per cent of the total number of patients of all ages with acquired lesions quired syphilis was commoner in girls than in boys.

The method of infection could be determined in 81 instances. Attempted sexual intercourse was the commonest method, but kissing and close contact, especially between mother and child, were other routes of infection. It seemed probable that the chances of acquiring the disease from infected household servants or food handlers were relatively slight. It was interesting to note that transfusion of infected blood caused the disease in 9 children and the necessity of testing all donors including parents was emphasized.

The course of the acquired disease resembled that in adults as a rule and responded favorably to the regular antisyphilitic therapy

Age in	WHITE				Total		
Years	Male	Female	Total	Male	Female	Total	
Under 1 1- 2 3- 4 5- 6	0 2 9 5 3 4	2 7 8 3 9 4	2 9 17 8 12 8	1 6 3 5 5 4	0 5 9 10 8 13	1 11 12 15 13 17	3 20 29 23 25 25
Total .	23	33	56	24	45	69	125

(Smith: Am J. Syph, Gonor. & Ven. Dis.)

TABLE 13

THE MODE OF INFECTION OF ACQUIRED SYPHILIS ACCORDING TO AGE ON ADMISSION

The Type of Lesions	Lesion with	Location of Primary Lesion with or without Subsequent Secondary		Latent	Transfusion	Total	
Age on Admission	Extra- Genital	Genital Including Anal	Demon- strable Primary			2004	
Less than 1 yr . 1- 2 yr 3- 4 yr 5- 6 yr 7- 8 yr 9-10 yr	1 10 7 5 6 2	0 3 11 11 8 13	0 5 10 5 8 7	0 0 1 1 1 1	2 2 1 0 2 2	3 20 30 22 25 25	
Total	31	46	35	4	9	127	

(Smith Am J Syph, Gonor & Ven Dis)

TABLE 14

THE METHOD OF CONTRACTING ACQUIRED SYPHILIS AMONG 125 CASES

	Sex of	Child		
Syphilis Acquired By	Male	Female	Total	
Sexual Intercourse: With Adult With Playmate Rape Pederasty Fellatio Kissing Close contact Transfusion No source recorded	2 6 0 2 2 5 9 7	16 9 4 0 2 10 5 2 33	18 15 4 2 4 15 14 9	
Total	44	81	125	

(Smith Am J Syph, Gonor & Ven Dis)

Congenital Syphilis

The occurrence of congenital syphilis in only 1 of a pair of fraternal twins was observed by U. J. Wile and D. G. Welton.²⁹¹ The diagnosis was first made in the 1 patient when he was 18 years of age. He had changes of the teeth and long bones characteristic of prenatal syphilis. Involvement of his central nervous system was proved by neurologic signs and the examination of the cerebrospinal fluid. The twin brother was normal. The father was apparently free from the disease and the time of the onset of the infection of the mother was not known.

TABLE 15
THE LOCATION OF THE PRIMARY LESION

EXTRAGENITAL			GENITAL				
Location Lip Mouth Tongue Tonsil Face and nose Neck Sternum Thigh	Male 10 1 0 1 2 1 1 1 1	9 1 2 0 0 1 0 1	Total 19 2 2 1 2 1 2 1 2 2 1 2 1 2	Location Vulva Cervix Perineum Glans penis Anus	Male 0 0 0 5 6	30 2 1 0 2	Total 30 2 1 5 8
Total	17	14	31	Total	11	35	46

(Smith Am J Syph, Gonor & Ven. Dis.)

Of her 7 pregnancies only the last, involving the twins and possibly the second, were productive of syphilitic children. The method by which 1 placenta and not the other of a twin pregnancy could

striking defects were the diminished size of the incisor teeth which was noted in 7 children, defective enamel in 5 children, and horizontal grooves in 1 patient. The 8 incisors, 4 cuspids, and 4 permanent

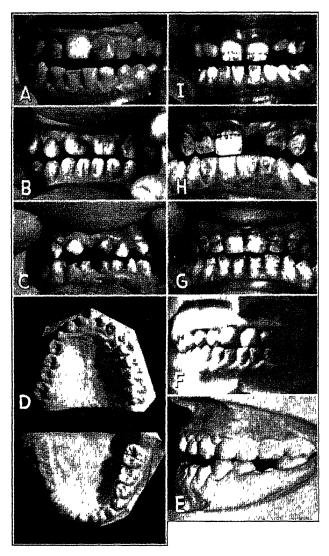


Fig. 18—Photographs illustrating characteristic dental detects. In A, B and C are seen the anterior regions of dental structures with detects of slight, moderate and marked degree, respectively. D shows a plaster model of the teeth seen in C. E and E picture plaster models which show the open bite deformity. G, H and I illustrate detects associated with tickets. (Anderson Am. J. Dis. Child.)

become infected from the mother was questionable

Some of the *dental defects* produced by congenital syphilis have been described by B. G. Anderson.²⁹² In 8 patients, 12 to 27 years of age, the most

molars were most frequently involved. The convergence of the walls of the tooth toward the incisal edge was the most constant defect of the upper central incisors and a somewhat similar change could be detected in the second incisor

and cuspid teeth. The most striking results of the dental deformities were malocclusion whereby the front teeth did not close properly, producing what was termed as an open bite. This resulted from poor development of the teeth and not from dental distortion nor any deformity of the jaw. Syphilitic deformities

and B. Pearson.²⁹³ The typical lesion was a yellow plaquelike band surrounding the intestine and consisting of miliary syphilitic and abscesslike foci in the mucosa and submucosa, with vasodilatation of the surrounding areas. Necrosis and, later, fibroblastic proliferation occurred. Sometimes ulceration and per-

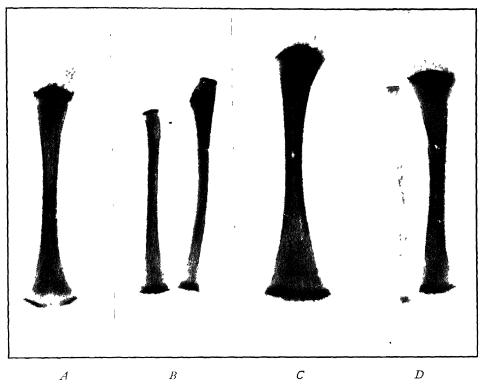


Fig. 19—X-ray photographs of the humerus, radius, ulna, femus, tibia and fibula taken from Baby T., No. 599, stillborn. The ends of the bones show the characteristic projections. Notice that they are absent at the slow growing ends of the upper ulna, upper radius and lower humerus (Park and Jackson. J. Pediat.)

must be differentiated from those caused by rickets. In rickets, the lesions are more apt to have a symmetrical distribution involving the parts of the teeth that are calcifying at the time that the disease is active. Rickets does not cause occlusion deformities because the teeth, though damaged by the disease, usually reach their normal size (See illustration.)

The pathologic changes occurring in the intestinal tracts of 3 syphilitic infants who were stillborn or lived only a few hours have been described by R D'Aunoy foration of the bowel led to peritonitis, but peritoneal irritation was sometimes observed without rupture of the gut Spirochetes were isolated from these typical lesions of the gut. The involvement of the intestinal tract has been observed most frequently in very young infants who have overwhelming syphilitic infections and usually in association with other visceral syphilitic lesions. The small intestine and especially the lower part of the ileum were the most frequent sites of these syphilitic lesions.

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Characteristic roentgenologic changes of the ends of the long bones of syphilitic children have been described E A. Park and D. A. Jackson.²⁹⁴ Irregular projections of the end of the shaft extended into the cartilage in some instances, usually at the rapidly growing ends. In the ribs the projections were longer and sharper than in the extremities. In both

between these areas. The accompanying pictures illustrate some of these roent-genologic changes.

Diagnosis—Changes in the serologic reactions of 56 infants during the first weeks of life have been evaluated by J. A. V. Davies.²⁹⁵ He employed a modification of the *Hinton test* which permitted the use of only very small amounts

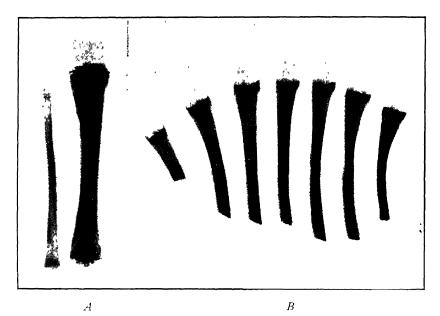


Fig. 20—A, x-ray photograph of the tibia, and fibula of a syphilitic infant, Baby B, No 300, aged 6 hours. The ends show a scalloped type of irregularity

B, x-ray photograph of a middle tier of tibs taken after death from I N, No 517, aged 1 day, showing a sample of the kind of changes at end of ribs which occur in congenital syphilis. (Park and Jackson J Pediat)

locations the ends of the bones were unusually dense. This condition had been noticed in 48 children of a series of 77 who had congenital syphilis. Almost all of these patients were infants less than 2 weeks of age so that the changes seemed to occur most frequently at an age when bone growth was most rapid. It was noted more rarely in older infants. The pathological structure indicated that bone growth of these patients had occurred along the nutrient vessels which extended into the cartilage, and there was a failure of calcification with evidence of degeneration of the cartilage.

of blood serum (005 cc) The flocculation was observed under low power magnification of the microscope and the strength of the reaction was determined by the density and firmness of the flocculation at the meniscus The positive reactions obtained in the newborn often reflected the reaction of the maternal serum. When the mother's blood was strongly positive, the infant's blood was usually strongly positive also A transmitted positive reaction of 25 infants usually disappeared within 2 weeks after birth but was noted in some instances to last for 6 to 12 weeks. Of a series of

11 such infants followed for a period of 6 months, only 2 developed evidence of congenital syphilis. Infants whose blood was negative from birth to the age of 6 months remained free from syphilis. In

The disappearance of a positive reaction within a few weeks did not necessarily indicate freedom from syphilis and the development of 1 or 2 positive reactions after an initial negative one should be

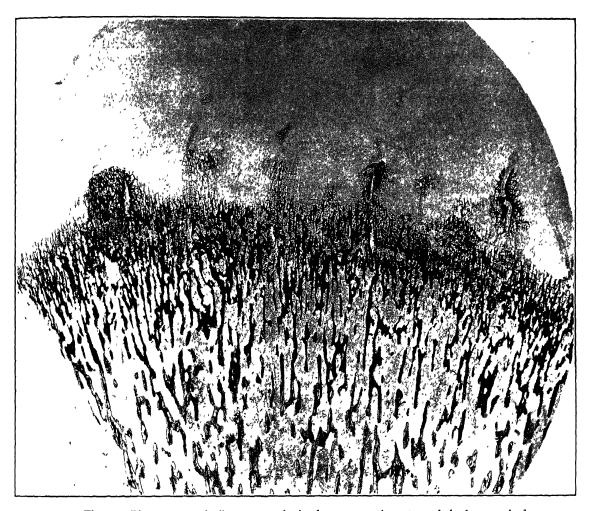
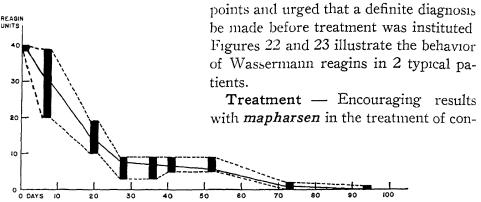


Fig. 21—Photomicrograph (low power view) of a microscopic section of the lower end of the femur seen in Fig. 1. It shows plainly the cause of the irregular projections of the end of the shaft into the cartilage. They are due obviously to building up of calcification about the vertical branches of the cartilage canals in advance of elsewhere. The canals are much hypertrophied, as is evidenced by the fact that they show so well at all places in a section in a single plane. The calcified matrix stains black. The network formed by it in toto is the syphilitic lattice. The preparation makes clear that the projections are merely extensions of the lattice (Park and Jackson: J. Pediat.)

1 syphilitic infant the initial positive reaction disappeared before his own reagins developed in sufficient quantity to produce a positive reaction. The author concluded that the newborn with positive serologic reactions should be observed especially closely for a period of 1 year considered as very strong evidence of actual infection of the infant

In a review of the various procedures for the detection of congenital syphilis in a young infant, W C Black²⁹⁶ has emphasized the fact that a diagnosis may be established within the first 3 months

of life by the frequent repetition of laboratory procedures. Dark field examination of umbilical cord scrapings or suspicious cutaneous lesions may give the earliest proof of the infection and roentgenologic



while the infants with syphilis who may

have negative reactions at birth will usually develop reagins during the same

period of time. The author reported the

histories of 3 patients illustrating these

Fig 22—(ase 1 Wassermann reagin titrations in a seropositive nonsyphilitic infant. The black columns indicate possible range of reagin as determined by serum dilutions tested. The solic line approximates the probable true course of the serum reagin concentration, the broken lines indicate the theoretically possible maxima and minima. (Black J. Pediat.)

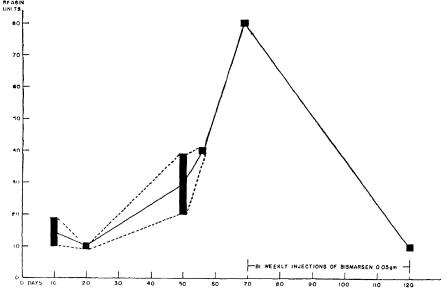


Fig. 23—Case 2. Wassermann reagin titrations in a case of proved congenital syphilis (Black: J. Pediat.)

evidence of bone lesions may lead to the diagnosis within the first few weeks of life. The accompanying tables include the criteria for making the diagnosis and for establishing the absence of the disease. Falsely positive serologic reactions of the newborn will tend to disappear by the time the infant is 3 months of age

genital syphilis have been reported by V H Cornell and G D. Astrachan ²⁹⁷ The drug was administered intravenously to 31 older children and intramuscularly to 11 infants at weekly intervals *Bismuth* was also given during the period of treatment. General reactions which occurred in only 3 patients

TABLE 16

TENTATIVE CRITERIA FOR POSITIVE DIAGNOSIS OF CONGENITAL SYPHILIS

- I. Diagnosis established by dark-field examination (identification of 2 or more living *T. pallida* in dark-field preparations).
 - A. At birth
 - In scrapings of the wall of the umbilical vein near the fetal end of the umbilical cor
 - B After birth
 - 1 In material from skin or mucous membrane lesions
- II Diagnosis established by serologic tests (properly done on suitable material)
 - A. At birth
 - 1 High Wassermann reagin titer
 - 2. Wassermann reagin titer unequivocably greater than that of the maternal serum
 - B During first four months of life
 - 1 Negative test becoming positive
 - 2 Rise in titer on subsequent measurement of a positive serum
 - C After four months
 - 1. Strongly positive test (checked)
- III Diagnosis established by roentgenologic osseous examination (interpretation by a competent and experienced individual, preferably a radiologist).
 - A At birth
 - 1 Changes of the sort described by McLean's criteria 1, 3, 4, 5, 6, 7, and 8
 - B At 6 weeks or later
 - 1 Same as III, A, 1
 - 2 Definite progression of osseous lesions as compared with those seen at about the time of birth and reaching the stage of McLean's criteria 1, 3, 4, 6, 7, 8, and 10

(Black J Pediat)

consisted chiefly of vomiting and slight fever Albumin and hyaline casts were noted in the urine of 1 child for a short period of time. No local reactions occurred Syphilitic lesions such as skin eruptions and interstitial keratitis responded well to the therapy. In the 31 older children, serologic reversals were obtained in 8 patients after 34 injections of the drug and another group of 8 patients showed partial improvement of their blood reactions. Of the 11 infants, only 9 received adequate treatment and 4 developed negative Wassermann reactions. It was concluded that mapharsen was an effective antisyphilitic drug with a low degree of toxicity Further trial was advocated for this form of therapy in the treatment of congenital syphilis.

The results of acetarsone treatment of 187 children with congenital syphilis have been reviewed by D. M. Pillsbury and H. H. Perlman 298 Eighty-seven of this series were observed for more than 3 years, 116 for over 2 years and 145 for more than 1 year. The response of cutaneous and osseous lesions was good but interstitial keratitis yielded less readily to this form of therapy Serologic reversals were obtained in 70 per cent of the infants whose treatment was instituted before they were 6 months of age and in only 36 per cent of older children. These results were less satisfactory than those obtained in a smaller group of infants and children treated with arsphenamine and bismuth or mercury preparations. Reactions to acetar-

TABLE 17

TENTATIVE CRITERIA FOR ESTABLISHING THE ABSENCE OF CONGENITAL SYPHILIS IN UNTREATED INFANTS AND CHILDREN

- I. At birth
 - A. Nonsyphilitic mother
- II At 4 months
 - A. Two negative blood and 1 negative spinal fluid serologic reactions, properly done on suitable material
- III After 2 years
 - A. Two negative blood and 1 negative spinal fluid serologic reactions, properly done on suitable material

(Black: J Pediat.)

sone occurred in approximately 11 per cent of the total number who received the drug Most of the reactions were mild, consisting of nephritis, gastroenteric disturbances and forms of dermatitis. In about 5 per cent of the group, however, the severity or persistence of the toxic manifestations required permanent discontinuance of the drug

The authors were unable to find any evidence that the co-operation of the parents was any better when the oral treatment with acetarsone was employed than when injections of the other arsenicals were used. In both groups, the attendance at the venereal clinics was 51 per cent of that which was expected. There was some indication also that the acetarsone might not have been administered regularly by the parents at home since reactions occurred much less frequently in ambulatory patients than in those who were treated in the hospital wards.

The importance of an early diagnosis of congenital syphilis was emphasized because it was the early administration of antisyphilitic therapy which provided the highest percentage of clinical cures and prevented subsequent relapses. It is only by the routine serologic tests of infants that the diagnosis can be made in many cases.

Malarial treatment for interstitial keratitis has been found to be effective in the patients observed by C. R. Anderson and W. A. Wilson.²⁹⁹ Of a group of 22 patients ranging in age from 4 to 44 years of age, there were 16 who received malarial treatment for 8 to 14 paroxysms of fever and 6 received intravenous typhoid-paratyphoid vaccine injections until they had had 8 to 20 bouts of fever of over 103° F. (395° C.) Injections of an arsenical followed the courses of induced fever. There were 13 patients with acute forms of interstitual keratitis and 9 with chronic forms of the disease The response of both groups was much better to the malarial therapy than to the typhoid vaccine injections although some of the patients had not been followed for a sufficient length of time to determine the end results

The course of 45 congenital syphilitic children has been followed for 2 to 10 years by P J Howard 300 Six of these patients were less than 6 months of age when treatment with *neoarsphenamine* was instituted Since extensive syphilitic infection of the liver was usually present in this age group, 50 to 100 cc. of a 10 per cent glucose solution were administered before the arsenical was given in order to prevent reactions. All but 1 of

these 6 infants were cured by continuous treatment over a period of 20 to 96 weeks. Fourteen other children of the entire group were cured and 3 of these patients had had evidence of central nervous system involvement. Eighteen children had positive Wassermann reactions but no clinical evidence of syphilis at the end of 2 to 10 years after the time treatment was started. Seven children failed to respond to the therapy and 6 of these had involvement of the central

nervous system. The importance of early treatment was stressed by the author. Adequate treatment was considered to include 24 weekly injections of the arsenical and an equal number of a bismuth preparation in alternate periods of 8 weeks each. If at the end of a year the results have not been satisfactory, another year's therapy was advocated. Patients with syphilis of the central nervous system required prolonged drug treatment and the use of fever therapy.

TUBERCULOSIS IN CHILDREN

By Waldo E. Nelson, M.D.

Clinical Manifestations — Pulmonary—A case of bronchial occlusion due to tuberculous lymphadenitis is reported by L V Schneider 301 The symptoms at onset were those of a "cold" with fever and difficult breathing. The asthmalike symptoms suggested the possibility of an asthmatic condition as well as the possibility of a foreign body or of bronchial stenosis due to other factors. Physical examination revealed an impaired percussion note, bronchial breathing and increased vocal resonance over the right upper lobe posteriorly and in the axilla The breath sounds were increased in intensity on the left side, musical râles were present in both lungs, and there was a loud inspiratory stridor with some retraction of the chest. A roentgenogram of the chest revealed an opacity of the upper half of the right lung. There was also a large circular area of opacity in the lower right with mottled infiltration about these areas Bronchoscopy showed the right bronchus to be somewhat distorted. The wall of the bronchus was rigid and somewhat thick, and the lumen was completely obliterated. The bronchus at the bifurcation was congested

and although the character of the pathologic lesions could not be determined bronchoscopically, it was not that of bronchial asthma. The possibilities considered were intrinsic stenosis caused by tumor, inflamed masses or scars and extrinsic stenosis due to pressure from tuberculous lymphadenitis. At autopsy a mass of tracheobronchial lymph nodes were found to be producing pressure obliteration of the right main bronchus with atelectasis of the right upper lobe.

Tonsils—A follow-up of 107 patients whose tonsils following tonsillectomy were shown to contain tubercules has been made by H. M. Pollard and A B Combs ³⁰² In the postoperative period, 3 patients developed active pulmonary tuberculosis; 1 developed tuberculosis of the cervical lymph nodes; and 1 developed tuberculosis of the spine. In 9 instances, pulmonary tuberculosis, present at the time of operation and in 3 instances tuberculosis of the mediastinal lymph nodes, also present preoperatively, were not diagnosed until the pathologists had submitted a report describing tubercles in the tonsils. In 20 patients in whom there was tuberculosis other than

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in the tonsils and adenoids at the time of operation, no additional tuberculous lesions developed. Seventy patients, without other tuberculosis at the time of operation, showed no subsequent tuberculous lesions. Of the 107 cases, the pathologists reported the presence of tubercles near the crypts in 56 instances

stage has developed. Then a dissemination of either the tubercle bacillus or some phase of its life cycle must occur. The type of cutaneous lesions depends on the site of embolism. If the smaller and finer arterioles become involved, the patient will have lichenoid tuberculosis. This is due to the fact that the hair

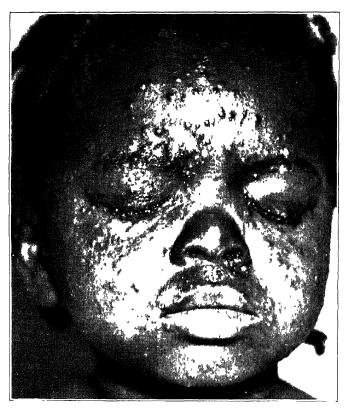


Fig 24—Case 3 Papulonecrotic tuberculosis of the face (Bernstein Am J Dis Child)

There were tubercles in the germinal centers indicating a hematogenous infection in 51 instances. It is obvious that every patient whose tonsils or adenoids are shown to contain tubercles should be carefully examined for tuberculosis in other parts of the body.

Skin Lesions — J C Bernstein³⁰³ points out that the mechanism of cutaneous exanthematous tuberculosis, while not definite, depends on several fixed factors. The patient must have had some form of tuberculosis, so that the allergic

follicles and sweat glands have a rich anastomosis of arterioles. If the larger arterioles in the cutis become involved, papulonecrotic tuberculosis develops. After thrombosis occurs and before canalization or collateral circulation is established, the tissue supplied becomes necrotic. After canalization and re-establishment of the blood supply, the lesions involute. When the site of thrombosis is in the larger arterioles or arteries deep in the cutis or in the fatty layer, erythema induratum develops. If many vestications are recommendated in the cutis of the fatty layer, erythema induratum develops. If many vestications are recommendated in the cutis of the fatty layer, erythema induratum develops. If many vestications are recommendated in the cutis of the fatty layer, erythema induratum develops. If many vestications are recommendated in the cutis of the fatty layer, erythema induratum develops. If many vestications are recommendated in the cutis of the cuties of the cutis of the cutis of the cutis of the cutis of the cuties of the cutis o

sels become thrombosed and large areas of tissue are deprived of their blood supply, necrotic ulcers develop and the question of healing depends on the amount of arterial damage. If many diffuse deep arteries become thrombosed, the nodose type of erythema induratum develops, and ulceration does not occur. Thus the entire clinical picture depends upon the amount of arterial damage, and while the various tuberculids have different gross morphologic descriptions, they are merely variants of one another and are all produced by the essential factors.

The ultimate outcome of generalized tuberculosis depends not on the cutaneous disease but on the extent of the visceral involvement. The author states that the prognosis for patients who have cutaneous tuberculosis is better than those who do not. The cutaneous lesions usually involute without other sequelae. An example of papular necrotic tuberculosis of the face is shown in Fig. 24.

Meningitis — The observations of M Gleich³⁰⁴ indicate that the Levinson test is of benefit in the diagnosis of tuberculous meningitis. In 30 cases of tuberculous meningitis, the Levinson test was positive in each instance; in contrast, none of 13 cases of nontuberculous meningitis had a positive Levinson test. It is pointed out that a positive Levinson test may be obtained with nontuberculous meningitic fluid which is contaminated by blood or the fluid of a patient previously given serum intrathecally

The Levinson test is performed as follows: 1 cc of spinal fluid is placed in each of 2 test tubes, 8 mm in diameter. To 1 is added 1 cc of a 1 per cent solution of mercuric chloride and to the other, 1 cc. of a 3 per cent solution of sulfosalicylic acid. The tubes are shaken, stoppered and allowed to stand at room temperature for 24 to 48 hours. At the end of this time, the column of precipi-

tate is measured in mm. When the height of the precipitate in the first test tube is at least twice that of the precipitate in the second test tube, the test is positive.

According to J. A. Toomey, R. P. Fulton and F. W. Rea,³⁰⁵ the tryptophan test is valueless as an aid in differentiating tuberculous from other forms of non-tuberculous meningeal irritation.

Diagnosis — Tuberculin — In 1937, H. Vollmer and E. W. Goldberger³⁰⁶ introduced a new tuberculin patch test which they claimed to be as reliable as, if not superior, to the Pirquet test. The tuberculin patch test as previously described has now been modified (1) by the use of tuberculin produced from a synthetic medium which is about 4 times stronger than the old tuberculin prepared by the New York Department of Health which was formerly used, and (2) by the use of 2 squares of filter paper saturated with tuberculin on each piece of adhesive tape, instead of the single square used in the earlier experiments with the test 307

Studies to determine the efficiency of the tuberculin patch test (Lederle-Vollmer) have been carried out by these authors.³⁰⁸ Among 417 children, the reliability of the tuberculin patch test as compared with the intracutaneous test performed with 0.1 mg of old tuberculin was 100 per cent. Among 261 tuberculous children there was complete conformity between the tuberculin patch test and the intracutaneous test with the first strength solution of purified protein derivative (PPD) or with 001 to 1 mg of old tuberculin. They suggest that the tuberculin patch test (Lederle) should replace the first intracutaneous injection in routine testing. Negative reactors to the patch test should be retested with the intracutaneous test with 1 mg (01) cc of dilution 1 to 100) of old tuberculin or 01 cc of the second strength solution

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(0.005 mg) of purified protein derivative. Since higher concentrations of tuberculin occasionally cause pseudopositive reactions, both tests are repeated if there is any discrepancy. If the discrepancy persists, the authors advise accepting the result of the intracutaneous reaction as the deciding one. A positive reaction to the patch test is illustrated in Fig. 25

A tuberculin test with an "immediate reaction" is described by H Sutherland.³⁰⁹ The test consists simply of

tuberculin. The reliability of this test, however, needs further confirmation.

The dangers of undesirable tuberculin reactions from too high dosages are emphasized by H Behrendt.³¹⁰ He cites instances of severe local reactions with necrosis at the site of injection, of general reactions, such as high fever, chills, urticaria, etc; and of focal reactions in tuberculous lesions of the viscera. This latter group constitutes the most serious danger and is in itself a sufficient reason for caution against employing too large

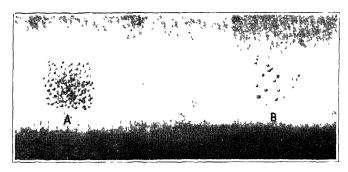


Fig 25—Photograph showing a positive reaction to the patch test. A represents a 2 plus reaction, B, a 1 plus reaction. (Vollmer and Goldberger. Am. J. Dis. Child.)

pricking the skin through a drop of undiluted tuberculin. The reaction, a white wheal about 5 mm in diameter, appears within approximately 5 minutes ordinary crythematous and indurated reaction is noted on the following day. In performing the test, the skin of the forearm is cleansed with alcohol and dried A drop of phenolized physiologic saline is placed on the skin and a few centimeters away is placed a drop of undiluted tuberculin. A prick through the superficial layers of the skin is made through each of these solutions, care being taken to avoid bleeding. The physiologic saline serves as a control to eliminate the possibility that a wheal reaction might be due to dermographia. The advantage of such a test is obvious, in that the patient would need make only a single visit to determine sensitivity or lack of it to doses of tuberculm. The author does not minimize the use of tuberculin for clinical testing, on the contrary, he states that in his opinion it cannot be dispensed with However, he emphasizes certain important points: (1) The initial test should always be with a low dosage if the intracutaneous method is employed, or the Priquet or patch test should be applied. When no reactions are obtained, higher doses may be applied by the intracutaneous method (2) A child who is known to be tuberculin-positive need not be retested with tuberculin.

Active tuberculo-protein stimulates the formation of monocytes and some epithelioid cells. The addition of phosphatide to the protein brings about a massive formation of epithelioid cells. With the increased cellular reaction to the mixed injections may be correlated the increase

in the speed and intensity of the sensi-The intradermal route is the best for the injections, probably because it provides the greatest dose per cell of the sensitizing agent. The differences in effectiveness between sensitization by the intradermal route, in contrast to the lining of the peritoneal cavity or the subcutaneous tissue is expressed by the following observations Using the peritoneal route of injection, the minimal amount of protein necessary to sensitize a guinea pig was 30 mg. (Seibert), by the subcutaneous route, 5 mg (Smithburn, Sabin and Geiger); by the intradermal route, the amount can be reduced to 0 025 mg when enhanced with phosphatide. The degree of sensitization artificially obtained by the synergistic action of tuberculo-phosphatide and tuberculoprotein is quite comparable to the degree of sensitization naturally occurring in tuberculous animals Moreover, this degree of sensitization may be induced with amounts of the materials from the bacilli which could conceivably be present in the tissues of an infected host

Differential Diagnosis — The sinilarity of infection with coccidioides fungus to tuberculosis is pointed out by E. C. Dickson 311. As in tuberculosis, there are 2 distinct stages A primary acute respiratory infection, often accompanied by erythema nodosum, from which the great majority of patients recover without complication, and a second stage consisting of a more or less chronic granulomatous disease, known as coccidioidal granuloma. This latter stage has a case mortality of approximately 50 per cent The initial or primary stage of the coccidioidal infection may be confused with primary infection with the tubercle bacillus and coccidioidal granuloma is often confused with reinfection tuberculosis. In the primary stage of coccidioidal infection patients are usually ill from 3 to 6 weeks. Frequently they are not sufficiently ill to call for medical aid; in fact, it is often pain from erythema nodosum which causes them to call a physician. At the onset, the symptoms are often those of a cold or of "flu," there being general malaise with fever and at times general aches and pains. There may be pleuritic pains Loss of weight may be rapid up to 15 or 20 pounds and there may be chills and sweating Temperature may range from 100° to 104° F. (37.8° to 40° C.). The bronchitis may be relatively mild but usually there is mucopurulent sputum which is sometimes streaked with blood The skin lesions are most commonly situated on the shins and are typical of erythema nodosum Similar lesions may appear on the thighs, buttocks, and upper extremities, when they simulate erythema multiforme. Roentgenograms of the chest during the acute attack usually reveal dense shadows in the hilar regions indicative of enlargement of the hilar lymph nodes Radiating out from the hilar regions and more or less widely distributed through the lung area are densities indicating parenchymatous involvement which may occur in any of the lobes The typical spherules of coccidioides may frequently be demonstrated in the sputum Cultures and gumea pig injections are other laboratory aids which should be employed Coccidioidin (the specific skin test antigen) skin tests are not only positive but are relatively violent in the primary cases

Prognosis—From a review of their experience with childhood types of tuberculosis, H. A Rosenberg, E W Goldberger and K Nojima³¹² conclude that the prognosis of children over 3 years of age, admitted to their hospital with the childhood type of tuberculosis, is good. The tuberculosis mortality of 80 children admitted with an early, primary

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complex was 6.2 per cent The tuberculosis mortality of 275 children admitted with the diagnosis of tracheobronchial node tuberculosis was 2.2 per cent. This group is a selected one and does not include children under 2 years of age, when the mortality is high nor does it include children with disseminated tuberculosis

Infectivity of Primary Complex-W H. Feldman and A. H Baggenstoss³¹³ have conducted a study to determine the presence of virulent tubercle bacilli in chronic tuberculous lesions of the lungs and of the contiguous lymph nodes in human beings who have died of causes other than tuberculosis. Material from a total of 68 subjects was utilized and negative results were obtained in all but 1 case. They conclude that the lesions of the primary complex of tuberculosis, when definitely encapsulated and sclerotic, or caseous or caseocalcareous seldom contain virulent tubercle bacilli data suggest that in adults endogenous reinfection is unlikely to occur from lesions of the primary complex

Immunity Conferred by Primary Infection—The ultimate effect of tuberculous allergy, as measured by a positive tuberculin reaction, upon morbidity and mortality from tuberculosis has been studied by G. Herlitz 314. Two groups of children, the 1 consisting of positive reactors to tuberculin and the other of negative reactors, were followed for a period of time. On the basis of his observations, the author concludes that the child with a positive reaction to tuberculin has a greater chance of developing active tuberculosis and of dying of it than does the nonreactor to tuberculin

Experimental Studies on Immunity—The effect of a primary pulmonary tuberculous lesion produced by BCG on experimental pulmonary tuberculosis in rabbits has been studied by B. J.

Clawson.³¹⁵ These experiments illustrate the influence of an existing inactive primary pulmonary tuberculous lesion on a subsequent exogenous reinfection. A quick inflammatory response was noted. This tuberculous reaction, while more pronounced than in normal animals for a few days, was soon retarded and fell much behind the progress of the tuberculous inflammation in normal animals. This retardation or complete suppression was seen for as long as 110 days after the time of infection. It was felt that this protection could not be attributed to allergy alone, for in other experiments it had been noted that a marked degree of resistance could be produced artificially both locally and generally in the absence of allergy.

On the other hand, it was suggested that the quick inflammatory response was probably due, to a great extent, to existing allergy, since the local tissue response had been found to be greater in allergic immune animals than in nonallergic immune animals. It was considered that the allergy which was associated with other mechanisms of defense in these animals could be a factor in resistance by hastening the phenomenon of inflammation and bringing the phagocytic cells in contact with the living organisms more quickly. While allergy may without question in some cases destroy tissue to the extent of spreading the infection, it was suggested that increased resistance might be afforded by the allergic phenomena in bringing about the tissue defense more quickly

On the basis of these experiments the author suggests the possibility that a latent or healed primary pulmonary tubercle may be considered in most cases to have a beneficial aspect (resistance, allergy, or both) which in the majority of cases far overbalances the deleterious effects of allergy

The effect of preventing the development of hypersensitivity in experimental tuberculosis has been studied by R. H. Follis, Jr.³¹⁶ The lesions of animals infected with the tubercle bacillus and prevented from becoming hypersensitive by treatment with old tuberculin showed less caseation than those of control animals that developed hypersensitivity.

In some of the nonhypersensitive animals pulmonary lesions developed which were marked by an extraordinary proliferation of acid-fast bacilli. Since in the majority of the nonhypersensitive animals these lesions did not develop and since the same lesions were found in some of the animals of the control group shown to be hypersensitive, it was concluded that lack of hypersensitivity did not play a rôle in producing the lesions of this type.

Prophylaxis - Vaccination with BCG by the multiple puncture method has been performed by S R Rosenthal317 and the results by this method compared with those by intracutaneous injection Based on the percentage of infants inoculated who developed a positive skin reaction to old tuberculin, the multiple puncture method appears to be as efficacious as a single intracutaneous injection. In each instance there were 100 per cent positive reactions to old tuberculin after a period of 1 year Control infants who received no BCG did not react to old tuberculin, except in 1 infant who developed active tuberculosis Because the multiple puncture method gave equally as good results as a single intracutaneous injection, the author feels that the former is superior because, by this method, there is (1) no gross local lesion, (2) no suppuration of lymph nodes, (3) no appreciable scar; (4) ease in administration and thus wider applicability, and (5) smaller dose of vaccine needed It is believed that larger

doses are needed for the single intracutaneous injection than for the multiple puncture method because a large single dose causes at least partial obstruction of the draining lymphatics which hinders the absorption of the vaccine as well as the effects of the tissue response.

The multiple puncture method was performed by making 35 tangential needle pressures through a drop of vaccine (1 cc. equals 5 mg. of BCG) applied to the lateral aspect of the left arm (approximate dose: 600,000 bacilli).

Treatment—The report of F. B Stafford and V. L. Kelly³¹⁸ is of interest because of the good results which they attribute to preventorium care. This is in contrast to the adverse opinion to this kind of care so frequently voiced by Meyers, Stewart and their co-workers. A follow-up study made on 600 children discharged from a preventorium showed that all of the relapses after treatment occurred in children who returned to homes containing other cases of active This was interpreted as tuberculosis showing the great importance of preventing future contact with open infection. They also state that the amount of tuberculous infection present has a definite bearing on prognosis as shown by the fact that only 3.6 per cent of the latent cases relapse as compared to 30 per cent of cases with a definite diagnosis of tuberculosis. Thus, they believe the incidence of relapse may be fairly accurately estimated on the amount of demonstrable tuberculous infection and disease present, and the probability of further infections by contact with "open" cases On the basis of their observations they believe that preventorium treatment is of definite value to those children who have tuberculosis, especially in the latent form of the disease

Data concerning the value of the preventorium in the early care of children PEDIATRICS

with primary tuberculous infection, but without evidence of active disease, are also presented by J. B. Hawes, Jr. ³¹⁹ Of 700 children who had been in the preventorium during the decade from 1922-1932, it was found that only 1 child had since died of tuberculosis and that only 3 had developed clinical tuberculous disease. As a control group, 700 children of the same age group, race, and

location were chosen. Each child was a "contact case" and had a positive tuberculin reaction, had not been resident in the preventorium but had remained at home under the care of city tuberculosis nurses and physicians and in a few instances of their own private doctors. In this group, 10 had died of tuberculosis and 40 had developed clinical tuberculous disease.

WHOOPING COUGH

By Robert A. Lyon, M.D.

Diagnosis-Various diagnostic tests for whooping cough have been reviewed by A. B. Donald 320 The most certain method was the culture of the specific bacillus on cough plates. In a series of 530 patients, positive results could be obtained in 95 to 100 per cent of groups of children examined during the first 3 weeks of the infection, in 44 per cent during the fourth week and 7 per cent or less in later stages. In 16 cases in which bronchopneumonia occurred as a complication, positive plates were obtained in 11 during the third week of the disease and not in the other 5 patients who were admitted after the third week of illness. It seemed likely, theretore, that bronchopneumonia did not prevent the expectoration of the bacillus. In a few children the bacterial colonies were very few in number and occasionally atypical forms were noted, so that considerable care had to be taken in the examination of the plates Tests made at the time of discharge of 110 patients were all negative and no carriers were discovered.

The complement fixation reaction, obtained in 123 patients at various times during the illness was not generally positive until the third week of the dis-

ease. The majority of patients had positive tests in the seventh or eighth week of the infection so that this test had but little diagnostic value. Positive complement fixation reactions were obtained in a relatively high percentage of patients who had had the disease a few years previously. The exposure to pertussis of adults who had had the illness previously did not change their complement fixation reactions from negative to positive except in occasional cases.

Leukocytosis and the increase in the percentage of lymphocytes were valuable aids in the diagnosis of whooping cough from the second week onward, the figures reaching their height in the third week of the disease. The sedimentation rate, and the intradermal test with a suspension of the pertussis bacillus, were of little value in diagnosis.

Intracutaneous injections of pertussis vaccine were unreliable as tests of the immunity of patients to that disease in the groups observed by M. K. Bazemore and J. C. Williams 321 Injections of 0.1 cc. of pertussis vaccines of various types and strengths were given to 2 groups of 48 and 31 children respectively. Reactions of 1.0 cm. or more in diameter during the following 72 hours were con-

sidered positive. No definite correlation could be found between the results of the tests and the history of previous attacks of the disease. Immunization of the susceptible children with the vaccine did not cause any constant reversals of skin reactions nor produce any evidence of an allergic response

Complications — The influence of whooping cough on tuberculosis was not great in the group of children observed during an epidemic by M. Siegel and E. W. Goldberger. 322 Whooping cough attacked a series of 25 children between the ages of 1 and 7 years, who had tuberculosis of various types. One infant died of tuberculous meningitis 4 weeks after the development of the paroxysms Two other children had exacerbations of their tuberculous lesions within 4 months after the beginning of pertussis The other 22 children remained well and there was no evidence that their tuberculosis had increased in activity Even in the 3 children with increased activity of the tuberculosis there was no direct evidence that the pertussis infection was the cause of the exacerbations Open pulmonary tuberculous lesions might be disseminated throughout the lungs by the bronchiogenic route during the paroxysms of the cough, but it seemed probable to the authors that well-healed tuberculous lesions were unaffected by whooping cough

In a review of the neurological complications of whooping cough, R. L. Nelson^{32,3} grouped the etiologic factors into 4 classifications of intracranial hemorrhage, spasmophilia, functional vascular lesions, and encephalitis. It seemed probable that the last mentioned cause was the most frequent in pertussis. The onset of symptoms of the central nervous system occurred most frequently at the peak of the paroxysmal stage of the disease and were most frequent in the youngest age groups of children. The commonest

symptoms were convulsions, vomiting, coma, disturbances of the superficial reflexes of various parts of the body, and paralysis of the extremities or of the muscles supplied by the cranial nerves. Ataxia, blindness and deafness have also been observed on rare occasions. Later manifestations of the encephalitis were psychic disturbances, somnolence, amne-

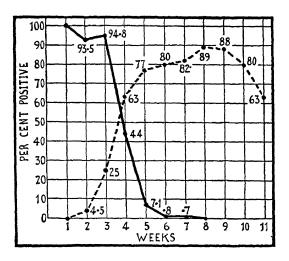


CHART 3—The continuous line represents cough plates, and the broken line complement-fixation tests (Donald Brit M J)

sia, mental depression, or retardation, spastic paralysis, and epilepsy.

The *treatment* of these nervous complications has usually been symptomatic, although the use of *convalescent whooping cough serum* has been suggested as a method worthy of further trial

Convulsions occurring in 41 patients with pertussis have been analyzed from a clinical viewpoint by K. Habel and P. F. Lucchesi ³²⁴. This complication developed most frequently in children less than 1 year of age and during the first 4 weeks, especially in the third week, of the infection. Associated symptoms were cyanosis, somnolence, or irritability before the convulsions began and a general collapse of the cardiovascular system, with an increase in pulse rate, a diminution of volume of the pulse, and a

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diminished blood pressure immediately after the convulsions. Complications of bronchopneumonia and otitis media occurred in 28 cases. Neurological signs were generally absent, although 3 infants had such residual disturbance as weakness of 1 arm, spastic hemoplegia and hyperactive reflexes with an erythema of 1 side of the body. The cerebrospinal fluids of 6 patients contained a number of cells, mostly lymphocytes, but in only 1 instance was the count greater than 100. The sugar content of the fluids was generally high, the chloride levels were within normal limits, and the bacteriological examinations were negative in all instances The total mortality rate of this series of patients with pertussis and convulsions was 78 per cent The pathological examination of the brains of 7 patients showed evidence of edema and distention of the cortical veins, but multiple petechial hemorrhages were noted in only 2 patients Treatment of the convulsive state was generally unsatisfactory and consisted usually of the administration of hypnotics or sedatives or the giving of ether in oil by rectum. The use of morphine was generally thought to be contraindicated because of the general collapse of the patient, calcium gluconate was employed without singular success; and the administration of pertussis vaccine to a few patients did not seem to change the course of the disease. The intravenous administration of whole **blood** seemed to be followed by the most striking clinical improvement and reduction in the mortality rate. The authors concluded that cyanosis might be a causative factor of the convulsions and that the early administration of oxygen by inhalations, barbiturates by mouth or otherwise, and immediate transfusion were the most satisfactory methods of treatment of this complication. In some extremely difficult cases one might resort to methods of reducing cerebral edema by the limitation of fluid intake, repeated spinal drainage and possibly by the intravenous injection of hypertonic solutions of dextrose.

Treatment—Sulfanilamide has been administered to 57 patients with whooping cough and the results were compared with those of a control group of 187 untreated patients by A. R. Thompson and C. R. M. Greenfield.325 The dosage of the drug varied from 7½ grains (0.5 Gm.) daily to children less than a year of age to 30 grains (20 Gm.) to children 10 to 15 years of age. Children with severe infections received larger doses, and occasionally the period of therapy extended for 8 to 9 weeks, without any reactions to the drug except cyanosis This therapy did not have any effect upon the paroxysms of coughing but seemed to reduce the incidence of such complications as pneumonia and otitis media. The drug also seemed to hasten the patient's recovery from bronchopneumonia when treatment started early. The series under observation was small and further trial with the sulfamlamide would be necessary before definite conclusions could be drawn

Immunization – Concentrated forms of pertussis vaccine for active immunization have been recommended by L. W. Sauer³²⁶ in a recent review of the status of whooping cough diagnosis and prevention. A double strength vaccine containing 20,000 million organisms per cc. may be used as subcutaneous injections in doses of 1 cc, 2 cc, and 2 cc. at weekly intervals, making a total of 5 cc. instead of 8 cc. for infants less than 2 years of age. For older children, 6 cc. may be necessary

Failures to produce immunity in children with vaccine have seemed to be the result of use of (a) impotent vaccines which are either prepared from old cul-

tures or have deteriorated because of improper refrigeration; (b) inadequate dosage; (c) improper technic of injection, usually too deep instead of just under the superficial skin layers; (d) failures of the patients to develop antibodies because they have been treated at very young ages; (e) exposure to the disease before immunity has developed; and (f) early loss of immunity because of intercurrent disease.

The effectiveness of various vaccines for active immunization against whooping cough has been investigated by M. Siegel.³²⁷ More than 1200 children received vaccine injections and approximately 1000 untreated children served as a control group. During a period of 14 to 23 months of observation, the incidence of whooping cough was approximately 36 per cent among the vaccinated children, and 42 per cent among the control groups. No true cases of the disease occurred in the children who received 80 billion bacilli in the vaccines prepared by the Sauer method or by that of the New York Department of Health less than 50 billion bacilli seemed to have little prophylactic value Intradermal injections of the vaccine were ineffective as compared with those given by the usual subcutaneous route. The difficulty in judging the results of vaccines in the prevention of a disease, such as whooping cough, is very great and even though the above series was a large one and adequately controlled, the number of children in each group to which the various vaccines were administered was small. The authors hesitated to draw conclusions in regard to the relative merits of different whooping cough vaccines and the various methods of their administration

Clinical observations of the results of prophylactic vaccination of a large number of children have been made over a

TABLE 18
INCIDENCE OF PERTUSSIS IN TEST AND CONTROL GROUPS BASED ON PERIOD AT RISK

	Groups in Study			
Time At Risk and	Both	In-	Control	
Subsequent Attack	Groups	jected		
Number of children Person-years Number of attacks Annual pertussis attack rate per 100 .	4212	1815	2397	
	4575	2268	2307	
	400	52	348	
	8.7	2.3	15 1	

(Kendrick and Eldering Am. J Hygiene)

period of years by P. Kendrick and G. Eldering.³²⁸ A group of 1815 children were vaccinated with pertussis vaccine and 2397 who were not injected, served as a control series. Both groups were observed over a period of 44 months. The vaccine employed was prepared from smooth, phase I types of pertussis bacilli recently isolated, and grown on a modified Bordet-Geniou medium. A total amount of 7 cc. of the vaccine was administered subcutaneously at monthly intervals in doses of 1 cc , $1\frac{1}{2}$ cc , $1\frac{1}{2}$ cc and 3 cc. respectively. Reactions consisted chiefly of local soreness and induration and occasionally some slight systemic symptoms Convulsions occurred in 1 patient and severe vomiting and relatively high fever in 2 other chil-The groups selected for vaccination were distributed fairly equally throughout the city of Grand Rapids and were fairly comparable in relation to sex, age, and the size of families

Of the total number of 400 attacks of whooping cough which occurred during the period of observation, 52 were in the vaccine-treated and 348 in the control group. Among the known exposures it was found that 128 per cent of the vaccinated group had been followed by attacks of whooping cough, while 685 per cent of the exposures in the control group had been followed by attacks of the

TABLE 19

Incidence of Pertussis in Test and Control Groups During Entire Period of Observation and by Quartiles of the Time Period

Quartiles 11 months each	Both Groups			Injected Group			Control Group		
	Person- Years	Number ot Attacks	Annual Attack Rate per 100	Person- Years	Number ot Attacks	Annual Attack Rate per 100	Person- Years	Number ot Attacks	Annual Attack Rate per 100
Total First Second Third Fourth	4575 157 440 1771 2207	400 6 28 86 280	8 7 3 8 6 4 4 9 12 7	2268 113 236 807 1112	52 0 5 10 37	2 3 0 0 2 1 1 2 3 3	2307 44 204 964 1095	348 6 23 76 243	15 1 13 6 11 3 7 9 22 2

(Kendrick and Eldering Am. J Hygiene)

TABLE 20
SEVERITY OF PERTUSSIS ATTACKS IN TEST AND CONTROL GROUPS

Severity Rating		Number and per cent of Attacks						
	Both Groups		Injected Group		Control Group			
	Number	Per cent	Number	Per cent	Number	Per cent		
Total attacks All attacks rated Very light Light Moderate Severe Rating unknown	400 395 35 95 218 47 5	100 0 8 9 24 0 55 2 11 9	52 52 21 17 12 2 0	100 0 40 4 32 7 23 1 3 8	348 343 14 78 206 45 5	100 0 4 1 22 7 60 1 13 1		

(Kendrick and Fldering Am J. Hygiene.)

disease. Some of the factors which might influence the effectiveness of pertussis vaccination were considered to be the type of vaccine, the length of its storage, the dosage employed, the time elapsing between vaccination and exposure to the disease, variations in the types of children studied and finally, the intimacy of the child's contact with the disease.

The minimizing properties of whooping cough vaccine depend a great deal upon the type of organism employed and the kind of media upon which it is grown G M Lawson³²⁹ has conducted a series of animal experiments with various kinds of vaccine. It was his conclusion that only the smooth types of pertussis bacilli which were intact and had

not been disrupted in any way, were the most effective forms for the production of immunity in animals only solid medium which was suitable for the growth of these bacteria was that originally devised by Bordet and Genjou Other types of media tended to cause a dissociation of the bacteria into avirulent forms. Various kinds of commercial vaccines differed in respect to the types of organisms employed and the consequent effectiveness in the production of immunity. Adequate dosage was also an important factor in producing the maximum amount of immunity. Sulfanilamide had no curative action against experimental pertussis produced in mice

The administration of pertussis vaccine to children who had received immunizing injections previously, greatly increased the immunity levels in the patients observed by Jui-Ping Wu and Fu-Tang Chu.³³⁰ Two infants were immunized according to the Sauer technic; a third patient had similar amounts of vaccine but with longer intervals (3 weeks) between injections and 2 other infants did not return for the third series of injections Agglutinins began to appear in the blood of all patients shortly after the second or third dose and then decreased in amount 4 to 19 weeks later Injections of 15 cc into each deltoid at this time caused a great increase in agglutinin titer and the repetition of this procedure 15 to 18 weeks later again caused a marked rise in the agglutinin content; much greater amounts being present than after the initial vaccination The author suggested a repetition of vaccine injection to immunized children who had been exposed to the disease.

Attempts have been made recently to increase the resistance of newly born infants to pertussis by administration of vaccine to the mothers J A Lichty, B Slavin and W L Bradford³³¹ have moculated 28 mothers with the Sauer type of pertussis vaccine during the last 6 weeks of pregnancy A series of 22 untreated mothers served as a control As a measurement of immunity to the disease, they employed a technic of determining the opsono-cytophagic reaction of the blood, which had previously been employed successfully as an index of the patient's resistance to the disease. The index was not increased in the mothers by the administration of the vaccine during pregnancy As a rule, the mothers' immunity exceeded that of their newborn but occasionally the infant's response was higher than that of its

mother. The opsono-cytophagic index was highest in infants whose mothers had had pertussis previously or had had the injections, and a combination of the 2 events produced the highest levels of immunity in the infant. Tests of infants before and after they had nursed during the first week of life showed no definite transmission of antibodies by way of the colostrum

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PHYSICAL THERAPY

by John S. Coulter, M.D.

ELECTROTHERAPY

Iontophoresis

Thrombophlebitis of Deep Veins—Sokolov and Meyers¹ treated 19 cases of the thrombophlebitis of deep veins with acetyl-beta-methylcholine chloride iontophoresis. The technic of the treatment was essentially the same as that of Kovacs It was found that a 0.1 per cent solution of acetyl-beta-methylcholine chloride was as effective as the higher concentrations previously recommended

Nineteen patients with thrombophlebitis of deep veins have been treated by this method by these authors. The shortest duration of the disease among the patients treated was 8 days, the longest 32 years Improvement was noted in 18 of the 19 cases The majority of the patients was able to return to full-time work, some at hard manual labor. Others were only partially rehabilitated In 1 patient pain and disability, which had been present for 30 years, completely disappeared Many of the patients had had various other forms of treatment over a period of years without relief.

Most marked improvement was noted in instances in which the disease was of not too long standing. When the disease had been present for a number of years improvement was slow and less dramatic. It is advisable to warn the patient that improvement may not manifest itself until several treatments have been given, else he may become discouraged and cease reporting for further therapy. It is not unusual, especially in the cases of old chronic phlebitis, to see no alteration in the disease process until a con-

siderable period of time has elapsed, and then suddenly to observe beneficial changes taking place. In fresh postoperative cases the results were at times quite dramatic.

Criteria of improvement were (1) diminution in the size of the limb as determined by measurements taken circumferentially at the level of the largest diameter of the calf and at the level of the malleoli; (2) improvement in ability to walk and stand; (3) ability to resume previously impossible occupations or tasks; (4) freedom or relief of subjective symptoms such as pain, heaviness of the legs, or "stiffness" of the legs.

Chronic Leg Ulcers-The same authors treated 13 cases of chronic leg ulcers of various etiology with the acetyl-beta-methylcholine chloride iontophoresis. In several cases the etiology was indefinite or possibly multiple, in at least 4 instances there was an underlying peripheral arterial deficiency. Two were pyogenic ulcers, 3 were varicose ulcers It was found in this small group that the treatment was apparently as effective in healing leg ulcers of other than varicose vein etiology as it was in the treatment of varicose ulcers. In many instances the patients had had previous therapy of various sorts without improvement In general, no other form of treatment was used concurrently with the administration of the iontophoresis.

One precaution which is observed in treating open skin lesions by the method of iontophoresis is that the ulcerated area itself is covered with a thin piece of rubber sheeting. If this is neglected there is likely to be concentration of the

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current at the point of ulceration, which may cause pain and further tissue destruction.

Clinical improvement in these ulcer cases was manifested shortly after treatment was started After 2 or 3 applications a healthy red granulation tissue appeared at the base of the ulcer Soon growth of epithelium became evident at the border, and by the end of 6 or 7 days measurable differences in the size of the lesions were apparent.

Short Wave Diathermy

The Council on Physical Therapy of the American Medical Association² in considering the indications for short wave diathermy state in part

Sprains—A mild sprain of the ankle can be satisfactorily treated by strapping to prevent lateral motion but not plantar and dorsal flexion. The efficacy of this method depends on the efficiency of the strapping. It is thought that plantar and dorsal flexion have a direct effect in promoting return of circulation and prevention of adhesions.

In the treatment of some sprains, fixation by a removable plaster splint and the daily application of heat and massage may be preferred. For immediate treatment, local applications of cold with rest, proper compression, bandaging and elevation are indicated. After the first 24 to 48 hours, there are local edema and decreased local metabolism Then the treatment should consist in removal of the splint and bandage followed by the application of external heat or diathermy, and this is usually succeeded by massage and exercise to produce a free flow of blood through the part

Bursitis—The first attack of bursitis can usually be relieved by physical therapy in about 2 weeks. The part should be placed at rest. For acute bursitis, infrared radiation from a luminous source

is given for 30 minutes at least twice daily and short wave diathermy is applied for 20 minutes once daily. As the pain diminishes, careful massage and relaxed motion should be employed; later, active exercise is started. Acute subacromial, radiohumeral, olecranon and prepatellar bursitis are treated in this manner.

For chronic subacromial bursitis, conservative measures, such as rest, infrared irradiation, short wave diathermy, massage and exercise should be tried before operation is considered.

Tenosynovitis — The treatment of traumatic tenosynovitis is to immobilize the joints whose motion causes pain in the tendons. The splint is removed and short wave diathermy is applied for 20 minutes once daily, followed by radiant heat once or twice daily for 20-minute periods. It may be advisable to use motion in a whirlpool bath to prevent adhesions.

Rheumatic, gouty and gonorrheal tenosynovitis are treated in the same manner as the traumatic form

Chronic Arthritis—Local heat may prove of great value, as may systemic applications, because of the alteration and improvement in the circulation brought about Great care should be exercised in the application of heat in cases of hypertrophic arthritis, since heat may constitute a form of trauma which aggravates the conditions already present. When indicated, however, local application of heat should be made from 2 to 4 times a day in the patient's room to produce an adequate increase in circulation, and, if medical diathermy is used, it may be supplemented with the former treatment When medical diathermy is used for chronic arthritis it should be used for a short period with low intensity for the first few doses, because sometimes it causes an aggravation of

the local symptoms. Clinical benefit, however, has been observed so often from diathermy that one should always give it a trial.

Fibrositis—This has been defined as a swelling and proliferation of the white fibrous tissue anywhere in the body in response to injury or very toxic infection, with a secondary effect of pressure on anterioles and nerve filaments. Heat, massage and exercise are used as adjuncts in the treatment, and diathermy may be used as one of the methods of giving heat.

Pelvic Infections — Some gynecologists use *medical diathermy* as one of the methods of applying heat in cases of pelvic infection, although most gynecologists believe that a low degree of heat usually suffices.

Respiratory Diseases—With bronchitis, medical diathermy relieves the pain and soreness in the chest, reduces the viscosity of the secretions and thus makes expectoration easier, it also relieves coughing

It has been observed that, in the management of pneumonia, medical diathermy does seem to be of definite benefit in reducing the severity of thoracic pain This symptomatic relief is inportant. The main factors concerned in the production of anoxemia are the passage of blood through the unaerated portion of the lung and shallow breathing. The shallow breathing may be due to pleuritic pain restricting the respiratory excursions The relief of this pain by diathermy increases the respiratory excursions and this may be the explanation for the decrease in cyanosis that is usually noticed There is no evidence that medical diathermy has a specific action on the pneumonic process

Gastrointestinal Diseases—For such conditions as acute enteritis, spastic colitis and simple catarrhal jaundice, ab-

dominal warmth is suggested as an aid in treatment. An electric heating pad or a hot-water bag kept on the abdomen for hours at a time is useful therapeutically. *Infrared irradiation* is a convenient way of applying heat; *diathermy*, if mild and properly applied, is also of benefit.

Inflammation of the Peripheral Nerves — With the various forms of neuritis, radiculitis and neuralgia, applications of heat may allay the inflammation and the pain. For deep penetration of heat into the tissues, medical diathermy may be used as a method of applying heat as an adjunct in general treatment.

Acute and Chronic Sinusitis—Infrared irradiation and medical diathermy are useful adjuncts to other treatment after adequate drainage has been established Medical diathermy is of value as an aid in the relief of pain, the frontal and maxillary sinuses are the ones most suitable for treatment

FEVER THERAPY BY PHYSICAL MEANS

Krusen and Elkins³ continued the observations of Krusen on this means of therapy These authors state that a carefully trained team consisting of technicians and a physician is essential to the safe conduct of fever therapy. The personnel of the fever therapy department is almost as important as the personnel of the operating room A competent physician familiar with all the reactions which can be evoked by this type of therapy should be in attendance at all times during the treatment. The treatment should be administered by registered nurse-technicians who have been trained for at least 1 month or 6 weeks in a well organized fever therapy

department of a hospital or under the close supervision of some person who has had such training. It has been said "The percentage of co-operative patients is directly related to the expertness and the tact of the nurse in charge." Failure to achieve a measure of success with fever therapy in many institutions arises from the fact that the attending nurses have not been adequately trained and are not familiar with the physiological principles that are essential to effective treatment. For many reasons the use of fever therapy should be confined to institutions. It must be borne in mind at all times that fever therapy is not without danger Though it is entrusted to a corps of highly trained workers, serious complications can and do occur during its administration.

Gonorrhea—The effects of artificial fever therapy produced by physical means on gonorrhea and its complications are conclusive. Reports by several investigators are available concerning the pyrexic treatment of gonorrhea is a large series of cases. More than 1000 cases of gonorrhea treated by artificial fever induced by physical means have been recorded during the past 5 years percentage of remissions in the series of cases previously mentioned has been approximately 90. The rationale of the application of fever therapy to gonorrhea has been based, of course, on the thermolabile properties of the gonococcus

Gonorrheal Arthritis—In most cases startlingly good results have been obtained with artificial fever in the treatment of gonorrheal arthritis. Most reports show that approximately 60 to 80 per cent of the patients become symptom free and that an additional 10 per cent are markedly improved; the other 10 per cent remain unimproved. The results are better when the treatment is instituted early in the course of the disease

than when it is delayed until the disease has reached a chronic stage. The procedure used in the treatment of gonorrheal arthritis is the same as that for gonorrhea in general.

Infectious Arthritis—About 30 per cent of 1 group of patients with infectious arthritis who were treated with artificial fever were significantly improved. The other 70 per cent exhibited little or no improvement. Fever sessions of short duration, during the course of which the bodily temperatures are elevated to from 101 to 103° F. (38.3 to 394° C) by means of *fever cabinets* and *hot baths*, have been used, in conjunction with other corrective physical therapy they have appeared to be of benefit

Syphilis (Early Primary)—Prelimmary clinical investigations seem to indicate that, when artificial fever therapy is combined with chemotherapy, better results can be obtained than by the use of either form of therapy alone However, in its present stage of development, fever therapy could not possibly be made available to the average patient having a primary syphilitic lesion When the bodily temperature has been elevated to more than 105° F (405° C) for 50 hours in 10 sessions of 5 hours each, this procedure being combined with 30 injections of an anti-syphilitic chemical agent, cutaneous manifestations of the disease, including chancres, have been reported to respond with surprising promptness, so that no living, motile spirochetes can be found in any of the primary lesions after the first fever treatment

MASSAGE AND EXERCISE

Chronic Arthritis — Fantus and Traut⁴ state there are 3 ways in which arthritis may be produced One is from

without (trauma or strain); another is from within (e. g., by infection). The third combines these 2, the effect of strain on a joint damaged by disease resulting in a vicious circle Other factors to the influence of which chronic arthritis owes its chronicity are endocrinopathies and subvitaminoses. Still more subtle is an inherited, constitutional inferiority of joint tissue. The therapy of chronic arthritis demands the breaking in on this vicious circle—the reason for its chronicity—at some point.

Today the profession is much less enthusiastic, dogmatic and drastic in its attack on foci of infection Certain it is that the time for their removal and the vigor with which they are attacked require considerable nicety of judgment. The patient must first be rested and built up

In all cases of chronic arthritis the physician must discover the reason for the persistence of the infection This is always due to poor resistance, which may be local or systemic; the latter may be hereditary or acquired. It is generally poor local resistance that determines the presence of foci of infection, and this is the reason such foci demand extermination Fantus and Traut believe that the patient's systemic resistance requires building up. The patient's food habits demand investigation, particularly as to his vitamin intake, for subvitaminosis lessens resistance. The diet should, in general, be low in carbohydrates. The Caloric requirements can be met with fats if the patient is emaciated Constipation and obesity demand diets with a high cellulose content to provide bulk as a peristalsis stimulant and to replace the hunger satisfying effect of foods of higher caloric value Patients with a history of "irritable bowel," "colitis" or tendencies to colonic distress and loose

stools require expert regulation of the cellulose intake.

Heliotherapy is just as beneficial in increasing the resistance in the arthritic as it is in the tuberculous. Living and sleeping outdoors is therefore ideal, provided the patient is not chilled and that he is carefully protected against sudden changes of temperature.

An abundance of **rest in bed** should be prescribed and its degree specified. This may vary from absolute rest in bed during acute phases of the disease to relative rest, e. g., an hour in bed in the middle of the morning with a nap directly after lunch or in the middle of the afternoon.

Physical therapy is much more important in chronic arthritis than is medicinal therapy. In the acute stages, **rest** and **heat** are indicated, while such evil effects of rest as weakening of the muscles and stiffening of the joints must be antagonized by appropriate **massage** and **active exercises**.

Local rest is demanded by any acute exacerbation of chronic arthritis

Heat is employed to relieve pain and stiffness, to induce relaxation before massage and to encourage certain poorly understood, favorable metabolic processes in the affected part Acutely inflamed joints should be exposed for an hour or 2 daily to a cradle containing 4 electric light bulbs, screened so that the patient cannot burn himself, or be wrapped in hot voluninous dressings of half-saturated solution of magnesium sulfate. A convenient method of the application of heat is the hot paraffin film.

Retentive appliances are important The prevention of deformity is much easier than its cure It demands persistent efforts to antagonize contractures

Massage should always be preceded by hyperemia (e.g, heat) and followed

by rest. When a joint is acutely painful either it should not be massaged at all or the lightest stroking only should be applied to the parts above and below the 101nt As soon as the pain is no longer severe, gentle friction (circular movement) and kneading should be applied. The muscles above and below the joint may now be given more vigorous treatment As tenderness disappears the joint itself may be treated more energetically; but this must never be to the extent of inflicting pain. Light active movements are allowable as soon as they are not accompanied or followed by pain. The aim of the exercises is to prevent adhesions and contractures, which often develop with great rapidity.

Exercise is encouraged up to the patient's tolerance. Marked fatigue or pain lasting into the next day is a sign that his disease-instituted limits have been exceeded. The patient is taught exercises especially adapted to the joints involved. Movements are often possible in warm water that are impossible out of it. Most patients are improved by the performance of such postural exercises as those of Goldthwaite and Osgood These exercises should be taught and frequently rehearsed. Typewritten instructions and record sheets should be employed to individualize better the patient's therapy Purposeful movements, exercise in making something (occupational therapy), are especially helpful in securing movement of particular groups of joints. This occupational therapy should also be developed in the direction of possibly teaching the patient a new means of earning his living, for, as in the case of tuberculosis, a return to the patient's previous mode of living often means the return of the disease

Green⁵ in discussing the orthopedic considerations in the treatment of ar-

thritis states that the measures during the acute phase are directed toward the maintenance of motion, combating atrophy in the muscles which are antagonistic to the deformity, and relieving pain Heat is helpful in allaying discomfort and as a preliminary measure to the exercises *Radiant heat* may be used, although moist heat is frequently more soothing in very painful joints. The latter may be given either with wet towels heated with a lamp for radiant heat, or by placing the patient in a warm bath such as the *Hubbard tub*. Prolonged heat is to be avoided.

If the Hubbard tub is used, exercises in water are given, always guided and active in type and directed toward decreasing the deformity. The temperature of the water is ordinarily from 98 to 100° F (367 to 378° C.). It may be a little warmer, although never over 104° F. $(40^{\circ}$ C), if the joints are very sensitive, or of lower temperature if the period in the water is to be quite prolonged. The buoying effect of the water is of great assistance, but too long a period in warm water is enervating and must be avoided. The movement of the joints must always be active or guided active, never passive. Passive motion increases spasm and pain, and does not allow as great a range of movement as do guided active maneuvers. The maximum are of motion that may be obtained without undue discomfort should be secured each day. Ideally, the range should be that which can be obtained painlessly, but a certain amount of discomfort is mevitable in most instances if function is to be preserved

The exercises need not be done in water If not, they should be carried out by a technician who supports and guides the part through its arc of motion, assisting in the extremes as sensitivity permits. At first, if the joints are

very sensitive, only 3 or 4 motions of each joint should be performed, but the exercises should involve all the possible directions of motion at the particular joint, always emphasizing motion opposite to deformity.

"Muscle setting" exercises are very useful in combating atrophy in muscles. They can be done by the patient without assistance and are not painful Since in "setting," the muscle is contracted with its origin and insertion closely approximated, the stimulating effect of the exercise is greater than would otherwise be the case. These exercises are particularly helpful in the instances of the quadriceps and gluteus maximus

Massage after the application of heat is a usual measure in conjunction with exercises and should be directed toward the atrophic muscles. Direct massage over sensitive joints is contraindicated.

If it is suspected that the exercises are too strenuous and are increasing sensitivity, they may be temporarily diminished in amount to determine whether they are an irritating factor. There are certain days when the joints are more painful than other, and activity on these days should be less. However, a certain amount of movement must be carried out, rarely should a day pass without some motion. An accurate record should be kept of the arc of motion existing in the various joints and particular effort should be expended in maintaining it

The correction of deformities and care during the very active phases are performed best in an institution. Once progress is being made and deformities are corrected, it is frequently possible to carry on at home. Some one in the household can usually be taught by the physiotherapist to guide the exercises twice a day. However, these must be checked at regular intervals by the clinician and the physiotherapist. The patient can

carry out some of the exercises himself, but many require help and supervision. Ideally a trained physiotherapist should supervise the exercises at all times, but in practice, they must be done in such an amount that some one living with the patient should be able to assist with them. Immobilization is practiced at home as indicated as long as there is activity.

As the process becomes quiescent, exercises become more strenuous Synovial thickening, sensitivity, and the general clinical picture, as well as laboratory determinations, are indices of activity. Walking must be attained gradually, and not before the muscles are strong enough to carry out their function. A therapeutic pool is of assistance when walking is started Various supports may be necessary, such as caliper braces and crutches Care should be given in the choice of shoes and frequently the feet must be protected by steel plates or flexible pads made in the form of an insole with the supporting factor either of felt or of sponge rubber If deformity has not developed and motion has been preserved, the problem of rehabilitation may be relatively simple Progress must be slow

Infantile Paralysis—Hansson⁶ states that the importance of rest and the protection of the weakened muscles have always governed the treatment of drop wrist, drop foot and other forms of peripheral paralysis. The Kendalls of Children's Hospital School of Baltimore have brought back the logical and rational view of the muscle re-education of patients with infantile paralysis have emphasized the neutral or ideal rest position for protection of the entire body. In the protection of the body they included prevention of any stretching or strain of weakened muscles This was accomplished by the wearing of protective supports, special care in handling the patient during nursing, and physical therapy. They also advocate restriction of the range of joint motion. Assistive movements were not allowed through the whole arc of function until the muscle was able to return actively to its shortened position. The Kendalls also advocated the use of heat, massage and pressure-suction treatment to prevent atrophy of the affected muscles

The objections to Kendall's treatment

- 1. If the regeneration of a nerve axon is at the rate of 0.5 mm daily, it will take 20 days to grow an axon of 1 cm, 200 days for 1 decimeter and 2000 days, or more than 5 years, for 1 meter. To keep a patient in bed with muscle protection for 5 years is neither humane nor practical.
- 2. Such long mactivity can hardly be imposed on a child without some psychologic injury.

The theory of the author of the after-treatment of poliomyelitis is that there is little or no difference between the treatment of poliomyelitis and any other lower neuron paralysis. There is but little disagreement as to the treatment of a dropped wrist due to radial nerve paralysis or a dropped foot due to paralysis of the anterior tibial nerve. In such cases one supports the weakened muscles, prevents any overstretching and maintains the nutrition and tone of the muscle by heat, gentle massage and reeducation exercises.

In this paper Hansson presents a study of 54 cases of poliomyelitis from the epidemic of 1931 in New York City. The patients were treated under his direction at the Hospital for Ruptured and Crippled and at the New York Hospital It is not an easy task to evaluate the recovery from poliomyelitis. Very few reports in medical literature actually

show the benefit of the treatment. The most valuable report is that of Legg, who studied 53 cases and showed conclusively that steady follow-up treatment lasting even 9 years is not only beneficial in preventing deformities but equally important in increasing muscle power. The subjects for this investigation were patients who were admitted to the hospitals between 1931 and 1935 and were followed at least 3 years. Their only treatment consisted in underwater exercises in specially constructed therapeutic pools. They were not selected patients.

In the calculation of the percentage of recovery, total paralysis was called zero and normal muscle 100 Any improvement from 1 grade to the nearest higher grade was therefore 20 per cent, and from zero to 100, or from total paralysis to normal, was 100 per cent On the muscle-testing chart used 19 muscles are listed in the lower extremity. Each muscle was tested, and the sum of the percentage of recovery of all involved muscles was divided by the number of muscles affected, which gave a percentage of recovery for the whole ex-The upper extremities and trunk muscles were graded in a similar manner

When this kind of calculation was applied in the 26 cases in which treatment was begun within 6 months of the acute onset, the actual muscle improvement taken as a whole was 2907 per cent, and in 28 cases in which treatment was begun 6 or more months after the onset the corresponding figure was 1639 per cent A comparison of the recovery of the various muscles shows that in the lower extremities the gluteus maximus, gluteus medius and dorsal flexors of the toes showed the greatest recovery and the tibialis anticus and posticus showed the least recovery. In the upper extremities the biceps showed a recovery of 80 per cent and the triceps the lowest recovery, or 29.5 per cent.

Hansson believes that the present consensus as to the aftercare of patients with poliomyelitis is better protection of the weakened muscles and less indiscriminate activity. He asks: "What is then the advantage of underwater exercise?" and "Should one continue to build more or less expensive therapeutic pools?" The answer to these questions is as follows:

- 1 The temperature of the pools ranges from 85° to 92° F. (295° to 33.3° C.), and thereby the application of heat, so necessary for the circulatory deficiency, is taken care of. Moist heat is better than dry heat, and the even distribution of heat through the contact of water is ideal
- 2 The water obliterates the effect of gravity and keeps the weight of an extremity from overstretching the weakened muscle. The motion of the extremity through the water probably produces the best form of massage, manual application of massage may do much harm by excessive pressure on the capillary stasis.
- 3 The exercises can be performed with just as much care under water as on a table. With the gravity eliminated one has the same resistance to movements in all directions. The physician owes a great deal to the Kendalls for having recalled to him the importance of protection during and after exercises.
- 4 Nothing can replace the therapeutic pool for the security that the patient feels when supported by the water

Volkmann's Ischemic Contracture

—Meyerding and Krusen⁷ state that it is only through the use of conservative stretching and surgical methods that benefit can be obtained in the treatment of long-standing Volkmann's contracture Without physical therapy, little can be accomplished In every case of ischemic contracture, whether operation is performed or not, physical therapy is the greatest aid in recovery of a useful extremity. At the Mayo Clinic a series

of 182 cases of Volkmann's ischemic contracture has been observed.

In the conservative treatment of Volkmann's ischemic contracture these authors state that Volkmann's ischemic contracture may occur in a few hours, and the earlier treatment is begun, the better will be the results. After relief of intrinsic pressure, no time should be lost in attempting gradual extension of the involved muscles. During the early stages, in the presence of edema and clots, heat and massage aid the absorption. After the deformity has been present for days or weeks, heat, massage, and gradual extension by splints are preferable, as by this time clots and swelling are subsiding.

If the patient is not seen for weeks or months after the onset of the contracture, plastic operative measures on the soft structures or plastic procedures on the bones must be considered. In cases in which the contracture is severe, operation may be the only means of correcting the deformity and postoperative physical therapy then allows further improvement. In all cases individual conservative treatment (that is, physical therapy) is applied at the same time, either without operative intervention if the patient is seen during the first week, or possibly following operative treatment if he is seen later With Sir Robert Jones' method the wrist is passively flexed to allow the fingers to extend and each finger is strapped in the extended position by means of a small guttersplint or by means of an ordinary tongue depressor. The patient thereafter immediately attempts systematic extension of the metacarpophalangeal joints which are contracted

In a few days the joints usually stretch sufficiently to allow the application of longer splints, which extend to the wrist. The wrist is still allowed to remain flexed and either a flat metal splint or a thin boxwood splint is used to flatten both the hand and finger. The wrist is then extended a little farther each day and held fixed in the corrected position.

Heat in conjunction with splinting, the use of other physical measures has never been sufficiently stressed. It seems wise to remove the splint once each day, in order that the other physical measures may be applied. Heat from a luminous source (such as a U-shaped baker containing 6 or 8 60-watt tungsten or carbon filament lamps, placed directly over the elbow, forearm, and hand, or a 250watt gas-filled tungsten lamp in a cupshaped reflector, placed at a distance of 2 feet from the elbow, forearm and hand) should be applied for 20 to 30 minutes Even better, the whole arm may be immersed for a period of half an hour in a whirlpool bath, which is a bath of whirling, aerated water kept constantly at a temperature of 110° F. (43 3° €)

Massage, properly applied, starting with light efflurage (stroking) and progressing to deeper petrissage (kneading) and to friction (a circular, rolling motion to loosen scar tissue and adhesions), may be applied by skilled hands. In the treatment of Volkmann's ischemic contracture, the time to be consumed by such massage will usually be about 10 minutes.

Manual manipulation of the affected arm and hand should be performed. This should consist of passive movements and active assistive exercises. While continuing careful stretching of the contracted muscles, the operator should progress as rapidly as possible to the stage of active assistive exercise (exercise in which the patient makes the voluntary effort to move the affected part and is aided in further motion by the operator). As the patient's condition improves, ac-

tive motions will become more and more established, and the assistive phase will diminish.

Finally, if and when function has been sufficiently restored, active exercise in the form of occupational therapy may be instituted. In Volkmann's ischemic contracture, 3 forms of occupational therapy are particularly indicated: (1) For the fingers, use of the hand loom, weaving, or basketry; (2) for the wrist, block printing; and (3) for the elbow, the use of a large floor loom, the affected arm being flexed and extended while at work with the beater of the loom.

Cardiac Conditions—Nylin⁸ believes that in the mechanotherapeutic treatment of cardiac conditions, rest is a very necessary complement to the exercises It is evident that a treatment with active exercises would only aggravate the cardiac condition of a patient whose heart had not enough reserve power for his daily routine activities. More than the usual amount of rest, and in some cases, a total curtailment of the patient's activities are, therefore, essential requirements in any program of exercise for cardiac patients Not only physical rest, however, but also mental rest are important elements these conditions Responsibility, worry, and psychic disturbances should, therefore, be avoided as much as possible

In regard to the selection and application of exercises, it is obvious that milder measures should be chosen and employed for patients with pronounced deficiency of the heart than for those with a certain amount of cardiac reserve power

When the most severe symptoms of insufficiency have been overcome, so-called "kneading" movements to the extremities should be added to the massage, and the passive exercises should be extended so as to include movements in the hip and shoulder joints. These ex-

ercises should be administered with a limited range of movement at first, the range being gradually enlarged according to the improvement of the patient.

When the reserve power of the heart has improved so that the patient no longer suffers from shortness of breath during rest, but the insufficiency continues to cause dyspnea and abnormally high or prolonged pulse rate and blood pressure after slight physical exertion, active exercises constitute the most important element of treatment. Active exercises may be in the nature of either free or resistive movements. Free active exercises are those that are performed by the patient without either resistance by or assistance from an outside force Resistive active exercises are those that are performed against the resistance of some outside force Of the 2 types of exercises, the resistive naturally place a greater amount of work on the heart

There are, however, certain definite rules which must be strictly observed in any program of exercise for heart patients

- 1 There should be an interval of at least 1 hour between a meal and the exercises
- 2 No exercise should be taken in the evening, as physical activity at that time easily may interfere with the patient's sleep
- 3 The treatment should be progressive in character—from tree active movements to resistive exercises
- 4 In the beginning the exercises should be taken with the patient in supine position. As the reserve power of the heart increases they may be performed in a sitting and finally in a standing position.
- 5 In the execution of the exercises it is necessary to take the force of gravity into consideration. For instance, in upward raising of the leg or the trunk with the patient in supine position, the weight of these parts offers considerable resistance to the movement. In order to prevent the exercise from producing a demand on the heart out of proportion to the cardiac strength, it is often necessary that the operator assist the movement. On the other

hand, while the patient is moving the leg or trunk back to the horizontal position, it is necessary that the operator give resistance to the exercise to overcome the aid to the movement produced by the force of gravity.

- 6 Depending upon the amount of cardiac reserve power, the exercises of the extremities should be performed unilaterally or bilaterally and with a limited or normal range of movement.
- 7. An exercise must not be repeated successively in the same part of the body. However, although it is not permissible to repeat an individual exercise in the same part of the body, the whole set of movements may be repeated if the patient's condition permits
- 8 All bilateral exercises of the arms that expand the thorax should be accompanied by inspiration, all those that compress the thorax by expiration.
- 9. A pause of 2 to 3 minutes should follow each individual exercise
- 10 Five to 10 deep respirations should precede and follow each whole set of exercises

It is advisable to consider after this the treatment for patients with a somewhat greater reserve power of the heart. To this group belong, among others, patients who are able to engage in mild physical activities and who can take prolonged walks on a level surface without becoming short of breath, but who become dyspneic on participation in somewhat more strenuous physical activities or upon walking up an inclined plane For this class of patients resistive exercises are of especial benefit. The movement may be administered with more resistance for this group of cases, and types of exercises producing a greater expenditure of cardiac energy may be employed

ULTRAVIOLET RADIATION

Intestinal Tuberculosis — Coulter and Hardt⁹ state that the literature on this subject is replete with data confirmatory of their own clinical experi-

ence, to the effect that the major trend of this grave disease, namely, pain, distention and diarrhea, is favorably influenced by general ultraviolet radiation in the majority of cases.

Although the diet as given by the authors is adequate in calcium for the normal person, it may prove deficient because of the extra losses of calcium from the tissues through the bowel and sweat glands. The good results obtained in this therapy may be due largely to the replacement of calcium in the tissues, together with its pharmacologic action. Direct exposure of the skin to *ultraviolet* light from the sun or from artificial sources forms vitamin D within the organism, but it should be borne in mind that the Council on Pharmacy and Chemistry does not recognize statements or implications that vitamin D has all the beneficial effects of exposure to sunshine

According to these authors it is reasonable to assume that when pulmonary tuberculosis is complicated by intestinal tuberculosis that relative avitaminosis and demineralization are likely to exist Therefore, the need of a high vitamin and high mineral diet for the relief of intestinal involvement becomes apparent It was their object to study the practical application of the value of a high vitaniin, high mineral, smooth diet, calcum therapy and heliotherapy. For the comparative efficacy of each principle they divided 315 patients into 8 groups They arbitrarily limited their study to cases that were under treatment for 6 months or more. The groups are as follows.

Group 1-A were given the high vitamin, high mineral, smooth diet, plus ultraviolet

Group 1-B were given the same as Group 1-A without the ultraviolet.

Group 2-A received calcium gluconate, 15 grains (1 Gm), by mouth a half

hour before meals, plus diet and ultraviolet.

Group 2-B received the same as Group 2-A without ultraviolet.

Group 3-A received $2\frac{1}{2}$ drams (10 cc) of 10 per cent calcium chloride solution intravenously twice a week, plus the diet and the ultraviolet.

Group 3-B received the same as Group 3-A without the ultraviolet.

Group 4-A received $2\frac{1}{2}$ drams (10 cc.) of 5 per cent solution of calcium gluconate intramuscularly 2 or 3 times a week, plus the diet and ultraviolet.

Group 4-B received the same as Group 4-A without the ultraviolet

The pulmonary condition of this group of patients roughly paralleled the intestinal condition. In other words the patients on the smooth, high caloric and high vitamin diet with or without calcium therapy plus ultraviolet radiation showed greater improvement than those with the same therapy without ultraviolet radiation This was contrary to the findings of Coulter and Carter. This apparently was due to the combination of diet and ultraviolet radiation

The criteria of gastrointestinal improvement are based upon a comparison of the symptoms, physical findings and laboratory examinations, including x-rays, proctoscopic and complete blood studies before treatment is instituted with those found 6 months or more after treatment

In brief, the general group of gastrointestinal symptoms at the onset of treatment included loss of appetite, nausea, vomiting, abdominal pain, diarrhea or constipation, or diarrhea alternation with constipation, loss of weight or failure to gain weight. The criterion of improvement is a marked decrease in the frequency as well as in the duration of the symptoms, or their complete amelioration, together with a decided gain in

weight, or at least a stationary weight. In a number of instances the gastrointestinal improvement apparently exceeded that of the pulmonary condition. The favorable change in the abdominal findings is characterized by a diminution or absence of rigidity and a lessening or disappearance of local tenderness. Slight to moderate localized abdominal physical findings may persist even after a marked weight gain and complete disappearance of symptoms. X-ray evidence of lessened bowel irritability usually accompanies symptomatic improvement and diminution of physical signs. This has been demonstrated in a number of instances by x-ray examination of the gastrointestinal tract 6 months or more after medical treatment has been instituted. The blood picture failed to show any definite changes characteristic of improvement In fact, in every group there was a slight tendency for the red blood count to decrease during the 6 months or more of treatment

Erysipelas—Knapp¹⁰ states that experience has taught us that the dosage should be very heavy so that the original dosage suggested by Ude, namely, twice the erythema dose, has now been increased to from 10 to 20 times the ervthema dose A border of 3 or 4 inches of normal skin around the involved area is included in the treatment. If multiple exposures are necessary the edges are allowed to overlap. If the evelids are not involved, the eyeballs are covered with black paper or cotton to prevent an ultraviolet conjunctivitis. If the evelids are involved and swollen, the patient is merely instructed to keep his eyes closed during the treatment Moist packs are prohibited for from 12 to 24 hours after the treatment, because they interfere with the proper development of the erythema.

Most of the patients remark about the relief of pain which often occurs while the lamp is still being applied. Later there is some increased edema of both the area of erysipelas and the surrounding normal skin. This subsides in from 24 to 48 hours, and if no further spreads or complications occur, the temperature drops rapidly to normal, the treated area wrinkles, then desquamates, and in 5 or 6 days the entire area is replaced with fresh-looking skin. In the majority of cases only 1 treatment is necessary.

In his conclusions the author states:

- 1 Ultraviolet radiation is an effective treatment for erysipelas
- 2. Reports from widely separated sections of the United States *i c*, New York City, Temple, Texas, and Minneapolis, Minnesota, comprising a total of 641 cases, show striking comparable results.

Willis¹¹ gives a comparative analysis of 60 cases of erysipelas with massive ultraviolet irradiation as an adjunct in treatment According to this author the first group of 30 cases was treated routinely with moist compresses, antitoxin and blood transfusions as indicated by the severity of the illness, and ultraviolet irradiation in small doses. The second group of 30 cases was treated with massive ultraviolet irradiation as an adjuvant to the treatment used in the first group

In a discussion of the methods used the author states

- 1 COLD MAGNESIUM SULFATE COM-PRESSES—Moist compresses have long seemed to be of value in inflammatory conditions. At least they appear to give the patient some comfort and have been used routinely in all our cases
- 2 Blood Transfusions—In all our cases of infants in both groups we have used **repeated transfusions of citrated blood**. No adults in the first group were given blood, and only 2 in the second group
- 3 Antitoxin In all the infants and the toxic children of our adult series, *antitoxin* has been used routinely. Many favorable and

unfavorable results have been reported following the use of antitoxin.

4 ULTRAVIOLET IRRADIATION — During the past few years we have been using with beneficial results ultraviolet rays in conjunction with other therapeutic measures in the treatment of erysipelas We had not, however, attempted using more than an erythema dose with slightly increasing daily exposures.

In January, 1935, we began using what seemed to us at that time excessive exposures to ultraviolet rays. Previous to this period we had used this same method of therapy, but no more than from one-half to 1 erythema dose with the light at a distance of 30 inches In our last group of cases the light was used at a distance of 10 inches and the patient was given 6 erythema doses. The light is used at this distance to take advantage of the short ultraviolet rays. The skin was irradiated 1 inch beyond the margin of the lesion. Most of our patients received 3 successive daily exposures. In treatment of the face it is important to cover the eyelids and lips in order to prevent burning of these areas with resultant edema and discomfort. This can be easily done with moist gauze flaps. In a very few cases it was necessary to extend the treatment over the routine 3 days. This depends entirely on the spread of the lesion. No allowance was made for infants or blondes, though they show greater sensitivity to ultraviolet rays. No case in our series received burns severe enough to cause sloughing of tissues. Only in a few was vesiculation noted, and this cleared nicely without further spread of the lesion

In the analysis of cases the author states that in their first group of cases there was a mortality of 166 per cent, which compares favorably with other reports including as many infants. In their second group the mortality was nil The

total mortality for the entire series of 60 cases was 8.3 per cent.

In the series of infants under 6 months the total mortality was 23 per cent. In comparison, Ude and Platou report a mortality of 633 per cent in 30 cases under 1 year. Nightingale and Starr report a mortality of 53.7 per cent in 95 infants treated with serum and ultraviolet In 59 of their cases serum was used with a mortality of 583 per cent. and in 23 cases ultraviolet therapy was employed with a death rate of 39 per cent McCann reports a mortality of 69 per cent in cases under 1 year. Rothman's series of 14 cases treated with blood transfusions shows a mortality of 28 per cent Elev reports 24 cases under 1 year with a mortality of 458 per cent treated by antitoxin

All the cases compared are under 6 months of age, averaging 3 and 28 months of age, respectively. The results obtained in our group seem very convincing, in view of the fact that all reports stress the age of the infant in determining the gravity of erysipelas

Our mortality rate of 20 per cent in 15 infants averaging 29 months of age and no deaths in the 8 infants averaging 28 months of age in Group II treated with massive exposures to ultraviolet is extremely convincing in comparison to other reports of a much higher mortality rate

It is not our belief that the excellent results obtained can be attributed solely to massive ultraviolet ray therapy, but rather to the proper application of the different methods of treatment used

Willis concludes that ultraviolet rays used in massive exposures give promise of great hope as an adjuvant to other methods of treatment in erysipelas and that ultraviolet rays have heretofore been used in ineffectual exposures.

Dermatology - Seborrheic Diathesis-Ingram¹² states that whether you are treating a simple affection like scurf of the scalp or a serious chronic seborrheic eczema and sycosis, it is important, first, that the patient should have any dyspepsia or constipation corrected and that he should be put on a diet. It is important, secondly, that any infection in the nose, throat and mouth should be eradicated. In this connection, a careful history, particularly as regards influenza, a direct examination, and a simple transillumination of the antra will generally indicate the presence or absence of infec-Thirdly, the nervous and psychological make-up of the patient must be given some consideration, particularly in relation to his environment and to any changes occurring at or before the onset of the skin affection Finally, it is desirable for the majority of seborrheics to adopt a strict toilet routine including a weekly shampoo, a daily bath, the use of a dusting powder and the wearing of cotton, preferably cellular cotton, undergarments This may sound a somewhat elaborate approach to what is no more than a rash, but a little thought will convince you that it comprises no more than the simple clinical overhaul which is called for in any constitutional disturbance

The disorders we have under consideration may be grouped under 3 headings. First, the simple infective disorders; secondly, physiological disorders; and, thirdly, the major constitutional seborrhetic disturbances.

The third group of affections consists of those which are essentially constitutional seborrheic manifestations. They include, first, eczematous symptoms. These may be localized or widespread and of the acute, subacute, or chronic type. Common examples are the eczemas

about and behind the ears; eczenias in flexures, especially the axillac, groins, and perineum; eczenias of the pompholyx types affecting hands and feet; and eczenia of the nape of the neck.

Less irritating than these nervous eczematous cases and generally very much more resistant and widespread, are the seborrhoeic eczemas dependent upon factors of malnutrition Blood counts, test meals and vitamin tests will generally indicate fairly marked degrees of malnutrition in these patients, and a case that Ingram illustrates, is a very characteristic example The patient had worked 8 to 9 hours a day for 6 days a week for a salary of 14 shillings. The author believes that such a case will indicate the great importance of the general outlook upon this problem rather than the more limited conception of seborrheic disorders as of external infective origin Dietetic treatment, the administration of iron and vitamins by mouth, general ultraviolet-light irradiation of the whole body and even the use of codliver oil as a local application to the skin are measures particularly indicated in this group

The last group of seborrheic eczemas is often associated with seborrheic svcosis, which is so distressing and intractable. The lesions are characterized by sticky, oozing, pustular, scabbed, and foul eczematous dermatitis in all the sites Ingram has previously mentioned, but particularly affecting the head and about the ears, the eyebrows, eyelids and beard Local treatment, even including x-ray therapy, is often without avail in all these cases They can be cleaned up with starch and boric poultices and fomentations, only to leave a fragile, red, glazed inflamed skin which within the course of another hour or 2 becomes covered with small subcuticular pustules

which, on the beard particularly, affect the hair follicles. All these cases show some degree of malnutrition, though it may not be of an extreme degree. What is, however, most important is chronic focal sepsis, generally affecting nose, throat or mouth, and this is hardly ever absent. The author is convinced that unless the provocative source of the trouble is satisfactorily dealt with these cases remain incurable. It is probable that any operative measures undertaken should be followed by anti-infective measures by mouth and general ultraviolet-light irradiation of the whole body, and any similar therapy likely to increase the patient's resistance to chronic infection

Bedsores—According to Cope,¹³ a bed-sore is an ulcer or area of impaired nutrition of the skin and subcutaneous tissues due mainly to the too great or prolonged pressure on those parts of the body that are most subject to pressure when the patient lies in bed

Preventive Measures—Avoidance of Undue Pressure—The author states that for this purpose it is necessary to see that the mattress is firm enough to prevent the body sinking deeply into it, and yet soft enough to allow it to be moulded to the contour of the patient's body A firm hair mattress is customary

Change of Posture in Bed—Normal people always change their position in bed as soon as any discomfort indicates the need for it. Sick patients cannot do this, so the nurse must do it for them in order to avoid too prolonged pressure on any one part

Avoidance of Minute Traumata—The greatest care must be taken to avoid slight injury to the skin when the bedpan is used; in persons who are recovering from an anesthetic and in those who are paraplegic it needs a careful hand and a vigilant eye to see that the skin is

not damaged by hot-water bottles. Dry bread crumbs or rucks in the sheet or drawsheet may cause unnecessary friction

Maintenance of Normal Condition of Skin—This is done by keeping it clean and dry, by massaging and in some cases hardening it. In an ordinary patient the pressure points are attended to twice daily (morning and evening) and after the bedpan has been used. In feeble patients and in those who are incontinent the toilet must be done every 4 hours or even every 2 hours.

Treatment of the Inevitable Bedsore—When, by the discoloration of the skin and the demonstrable lack of capillary circulation, it is recognized that a bedsore is inevitable, it is recommended by Latimer that the area be hardened by means of tannic acid solution.

When a definite sloughing ulcer is present it must be specially treated in one of the following ways. For small and even moderate-sized ulcers there is no doubt that the application of *elastic adhesive plaster*, as advocated by Carty, is useful.

There are still many who prefer to treat bedsores by the older-fashioned methods of astringent or antiseptic applications. There are many to choose from

In addition to local applications, healing may be hastened by the use of artificial sunlight or ultraviolet rays to the part. When there is a large slough it may be advisable to cut it away, but that is about as much surgical intervention as is ever required.

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ABDOMINAL SURGERY

Edited by James Norman Coombs, M.D.

Skin Disinfection — Scrubbing with brush, soap, and warm water reduces the basic flora at a constant rate. Irrespective of the initial size of the flora, the number of bacteria is reduced by approximately one-half with each 6 minutes of scrubbing The kind of soap used makes no difference. Variations in the temperature of the water used has no appreciable influence on the rate. The amount of vigor used in brushing is a very important factor, however Sterile water has been found to possess no advantage over ordinary tap water in reducing this flora

Ethyl alcohol has a very narrow range of effective germicidal concentrations. The optimum germicidal strength, both in vitro and on the skin, is 70 per cent by weight (not by volume as ordinarily prepared) At precisely this concentration, alcohol is more effective than any other hand disinfectant now in general use Each minute spent in this particular solution (at 77° F -25° C) has a cleansing effect equivalent to about 6½ minutes of scrubbing. This effect may be increased considerably by friction. i e, by rubbing with gauze or a washcloth.

Mercury bichloride solutions do not reduce the flora on the skin appreciably. Paradoxically, a sterile cutaneous surface may be produced. This phenomenon is due to the formation of a transparent "film" on the skin under which the bacteria are imprisoned. There, conditions

are so suitable to life that multiplication takes place, the existing flora doubling every 50 minutes. The "film" may be broken up, either with an alkaline sulfide or by prolonged friction, whereupon the bacteria are released uninjured.

The same phenomenon is observed when postassium mercuric iodide (biniodide) or Harrington's solution is used. Neither of these is a true germicide when applied to the skin. When used, these agents should always be followed by an alkaline sulfide

Kelly's method of hand disinfection (with hot saturated solutions of potassium permanganate and oxalic acid) is very effective. The procedure requires from 2½ to more than 5 minutes, depending on the temperature of the solutions. The total cleansing effects are equivalent to between 20 and 30 minutes of scrubbing.

Saponated solution of cresol, though a relatively strong germicide against test organisms in vitro, proved a worthless disinfectant of the skin

A search for a more nearly ideal hand disinfectant has resulted in the production of a new germicidal mixture which seems to possess certain advantages over any of the agents in general use. It is powerfully germicidal, each minute spent in it (at 77° F.—25° C.—without friction) being equivalent to more than 11 minutes of scrubbing. It is simple and pleasant to use. It does not irritate or injure the skin. It is more stable than

simple ethyl alcohol solutions. This germicide consists of ethyl alcohol, 50 parts by weight, normal propyl alcohol, 20 parts by weight, and water, 30 parts by weight. It may be prepared as follows: ethyl alcohol (95 per cent), 675 cc.; pure n-propyl alcohol, 250 cc., and distilled water, 250 cc., all measurements being made at 77° F. (25° C.).

Freshly prepared (U. S. P) tincture of iodine (7 per cent), applied to grease-free skin, comes nearer to full sterilization of the epidermis than any other germicide tested.

From bacteriostatic and bacteriocidal standpoints, mercurochrome is in many respects similar to the morganic salts of mercury.

Preoperative Preparation of the Hands—The following procedures are recommended.

- 1 The hands are scrubbed with soap, a good brush, and warm water for at least 7 minutes. This will usually suffice to remove gross dirt, transient bacteria and fats, and incidentally about half the basic flora.
- 2 The resident flora is much more effectively attacked by germicides than by scrubbing Ethyl alcohol, 70 per cent by weight, or the mixture of alcohol described is recommended These solutions should be freshly and accurately prepared Before entering the alcohol basin, the hands and arms should be dried thoroughly with a sterile towel, for to carry water into alcohol would weaken the solution and markedly lessen its germicidal power. In the alcohol basin the skin should be rubbed firmly with sterile gauze or a washeloth

The time spent in these solutions is of the utmost importance. Ethyl alcohol should be used with friction for 3 minutes by the clock, or the mixture of alcohols for 2. This may be expected to reduce the original flora from 50 per cent (result of scrubbing) to something less than 2 per cent.

- 3 Gloves and gown are put on. An ungloved hand inevitably increases the risk of wound infection
- 4 Between operations the hands should be washed in a germicidal solution in order to counteract the increase of cutaneous bacteria

which has taken place beneath the gloves. A useful rule is 1 minute in alcohol for every hour that the gloves have been worn.

Preparation of the Field of Operation—Before coming to the operating room the patient should receive a bath, the site of operation being especially well washed with soap and water to remove dirt, most of the fats, and any transient bacteria. If, as in the presence of a wound, this is not possible, a chemical detergent should be used.

Immediately before the operation, the site of the incision should be washed with gauze and 70 per cent (by weight) alcohol or the suggested mixture of alcohols It should be allowed to dry slowly, for in disinfection time is a factor that cannot be ignored

The alcohol is to be followed by one of the stronger germicides. U.S. P. tincture of iodine (7 per cent) is extremely effective. After application, iodine solutions should be permitted to dry slowly. Washing a dried coat of iodine off the skin with alcohol increases rather than diminishes the total germicidal effect.

As an alternative to the iodine technic, the field of operation may be painted with Scott's alcohol-acetone, 2 per cent solution of mercurochrome, or an irregular area such as that of a hand or foot may be soaked for a minute in 1:500 biniodide solution. In either case, an aseptic surface will be produced However, the line of incision must be first specially prepared (disinfected), else the knife will necessarily pass through bacteria-laden skin beneath the "film." One way to do this is to rub the site of incision for 2 or 3 minutes firmly with gauze and 70 per cent (by weight) alcohol or the mixture of alcohols

Disinfection of Contaminated Hands—It is not difficult to disinfect hands, contaminated by contact with in-

fectious patients or materials. The following method is recommended:

- 1. The hands should be washed as soon as possible with soap and running water for at least 30 seconds. This may be expected to remove about nine-tenths of the contaminating organisms. If there is pus, blood, secretion from the wound, saliva, mucus, or other infectious material on the hands, washing should be continued for a minute or more, perhaps with the use of a brush.
- 2. The hands should be well dried on an individual towel
- 3. Every part of the hands should be wet with 70 per cent (by weight) alcohol A few cc dripped on the hands will suffice The alcohol should not be wiped or shaken off but the skin should be allowed to dry by evaporation It is the germicidal action that is required, and that takes time.

Pathogenic Bacteria in the Air of Operating Rooms-In 1937, D. Hart published a report on the use of bactericidal radiant energy in operating rooms as a means of preventing infections by air-borne organisms The validity of his conclusion that most operative infections were due to air-borne contaminants was challenged in certain quarters upon the author¹ obtained the co-operation of 33 hospitals in 17 states for the study of bacterial flora in the air of operating rooms. This article is a report of the study, and includes a tabulation of the data sent in by the various hospitals, together with the author's comment

The average counts of bacteria were lowest in operating rooms which were equipped with air-conditioning systems, but even these averaged 35 colonies per hour of exposure of an agar plate. Hart claims that with the addition of bactericidal irradiation, the number of colonies per plate per hour can be reduced to 1 or less. The number of bacteria in the air increases in proportion to the number of occupants, particularly when any one of the occupants has a respiratory infection. Most of the pathogenic organisms

recovered were staphylococci, strepto-cocci being found only occasionally.

The author concludes (1) that pathogenic bacteria floating in the air and universally present in the occupied room are the greatest cause of infection in clean incisions in the modern, well-run operating room; (2) that air conditioning with forced ventilation will reduce the degree of contamination of the air, but will leave large numbers of circulating bacteria in the vicinity of the wound and the sterile supplies, most of them derived from the operating personnel; (3) that bactericidal irradiation of the air in the operating room is the only method available for achieving further reduction of air-borne infection

Acute Postoperative Circulatory Disturbances — In considering circulatory disturbances following severe operations, H Devine² distinguishes between (a) the patient who has a normal circulatory mechanism, and (b) the patient who starts out with some "crippling" of his circulation, either cardiac or peripheral A pre-existing circulatory crippling may introduce a large element of cardiac failure into a postoperative circulatory disturbance which might be regarded as a pure postoperative shock From a therapeutic standpoint, this is important, because the treatment of these conditions is diametrically opposite

Postoperative Circulatory Disturbance in Patients with a Normal Circulatory Mechanism: Shock (Sometimes Called Collapse) — Shock has many causes, for example, trauma, toxemia, anaphylaxis, hemolysis, and even psychic disturbances. These all give rise to a similar clinical picture; a sudden circulatory exhaustion, manifested by pallor, sweating, rapid pulse, rapidly falling blood pressure, increased respirations, and apathy

The author discusses 2 forms of shock: (1) That which appears during or immediately after operation, and which seems to have a neurogenic basis; and (2) the form which comes on secondarily, possibly because of some circulating toxic product or perhaps a sudden disturbance in the blood-clotting system.

Neurogenic shock can, to a certain extent, be avoided by careful handling of the tissues during the operation, and the judicious administration of the local or general anesthetic. It is sometimes wise to anticipate the onset of shock by an intravenous infusion during, or at the end of, the operation.

The treatment of postoperative shock in a patient whose circulatory system can be regarded as healthy is based on the following principles:

- 1. The blood vessels must be filled to compensate for the plasma loss and for the decrease in the amount of circulating blood. The author recommends a continuous drip infusion of from 8 to 10 per cent glucose in saline solution (Tyrode or Ringer) of approximately the same chemical composition as that of the plasma. A blood transfusion may be given if necessary.
- 2. The peripheral vascular system must be toned up, that is, contraction of the peripheral vessels must be stimulated. For this purpose, the action of adrenalin has been found to be too evanescent. Recently, however, several brands of synthetic adrenalin have been produced, sympatol and synephrin hydrochloride. These may be administered directly in the intravenous dextrose drip
- 3. The breathing center must be stimulated in order to hasten the circulation of the blood. Five per cent carbon dioxide in oxygen may be administered intermittently. When the breathing center is severely depressed, lobeline should

be added to the intravenous drip solu-

Postoperative Circulatory Disturbances in Patients with a "Crippled" Circulatory Mechanism - A study of the literature reveals that between 10 and 15 per cent of postoperative deaths are caused by a circulatory disturbance for which a pre-existing lesion of the heart is mainly responsible Frequently, this lesion may not be recognizable by means of the usual clinical examination. The diagnosis of how much peripheral vascular failure and how much cardiac failure play a part in a postoperative circulatory disturbance is important, for the principles of treatment of the cardiac failure component are diametrically opposed to those underlying the treatment of the peripheral vascular failure which is responsible for true shock.

The author discusses the differential diagnosis of postoperative peripheral circulatory failure (shock) and cardiac failure; the manifestations of the 2 conditions are the opposite of each other In cardiac failure, the blood pressure is usually not low; the venous pressure is high; the arm and neck veins are distended; the liver may be palpable; there are urobilinogen and albumin in the urine; the cheeks are not sunken as in shock, nor the eyes so deep set; the patients desire to sit up; there is an increase in the amount of circulating blood; and not nearly so much decrease in the systolic output as in peripheral vessel failure (shock). It must, however, be understood that in some cases cardiac failure may be secondary to a vascular insufficiency, and may be the result of an insufficient amount of blood offered to the heart by the peripheral circulation which results in an insufficient supply of blood to the coronary arteries and causes a definite injury to the cardiac muscle.

Treatment of Cardiac Failure—Cardiac stimulants which are suggested include caffeine, "cardiazol," "coramine," digitalin, and strophanthin. Mechanical aids to the circulation are also advised. These are (a) abdominal pressure (abdominal bandage or corset), (b) abdominal respiration, (c) stimulation of intestinal peristalsis, and (d) the upright position as soon as possible.

Morbidity from Operative Complications—Of the 450 patients that W. C. Beck³ observed for operative complications (wound infections and pulmonary lesions), 332, or 738 per cent, had an uneventful convalescence, whereas 118, or 262 per cent, had some complication during the postoperative course; only "clean" operations were selected for the study. In no case was more than I complication reported This may be due to lack of observation on the part of the person filling out the report but is more probably due to the fact that the present ing complication overshadowed the sec ondary one. There were 5 deaths in the Surgical shock and "gas pains" are not being considered. In the series there were 56 wound complications, most of which resulted from hematomas in the wound

When the edges of the wound are slightly raised and reddened, a hypodermic needle inserted into the wound will usually aspirate a small or moderate amount of old blood or of blood-stained purulent material, these are small hematomas rather than infections. Most of the 28 pulmonary ailments in the group were classified as bronchitis. Whether or not this minor bronchitis represented small areas of atelectasis is not in the province of this discussion. There were 8 lesions definitely classified as atelectatic. There were 13 patients with complications referable to the urinary tract

There was usually mild cystitis, although there was 1 instance of violent cystopyelitis which resisted therapy. Only 6 of the patients had had retention of urine requiring catheterization. The complication arose most frequently in young persons. Thrombophlebitis of the femoral vein occurred in only 2 persons in the entire series. The other complications were so inconstant that discussion of them is not indicated

Many factors enter into the pathogenesis of the complications To evaluate any one of them, all of the others must be kept at an absolute or relative value However, in reviewing the practical lessons learned from the study, the author finds that probably the most important is that an explanation can usually be found for a temperature which remains over (37.5°C) for more than 4 99 6° F days. If one is alert for this sign, he will be able to "pick up" far more of the complications which beset the surgical If the complications are faithfully recorded, a cause and a cure for some of them will undoubtedly be found

Abdominal Injuries

In a discussion of deep hematomas and chronic phlegmons of the abdominal wall causing difficult diagnosis, G. Balice4 states that deep hematomas of the abdominal wall are usually divided into spontaneous and induced hematomas The former occur without demonstrable cause or on the occasion of a minimal traumatism (cough) and appear nearly always in the sheath of the rectus muscle after rupture of the muscle and its vessels; the latter are caused without doubt by a traumatic lesion of the vessels. About 100 cases of spontaneous hematoma have been reported. The disorder begins like an acute abdominal disease, with intense pain, abdominal tension, and vomiting, while a rather soft tumefaction of varying size develops on either side of the median line above the level of the arch of Douglas and within the lateral limits of the rectus muscle. All kinds of acute abdominal disorders have been erroneously diagnosed in these cases.

Balice describes 2 cases of deep hematoma of the abdominal wall due to wounding of the lower epigastric artery in the course of a surgical intervention for inguinal hernia. Very few cases of this kind have been reported. In the first case the patient felt a sudden, rather acute pain in the region of the right iliac fossa 11 days after a Bassini operation; the pain soon disappeared. On the following day there was a tumefaction which was raised only slightly above the cutaneous plane; it was rather round, painless, and of somewhat elastic consistency, had a diameter of about 10 cm. and was deeply seated and nonadherent to the skin Contraction of the abdominal muscles made it disappear. A neoplasm was at first suspected, but upon puncture 400 cc of bloody fluid were delivered, and the patient was well within a few days. There seems to be little doubt that trauma of a vessel during the operation had caused late hemorrhage through some mechanism difficult to explain

In the second case the patient was admitted with the diagnosis of malignant abdominal tumor. He had been operated upon for strangulated inguinal herma 1 month previously and immediately after the intervention, had felt slight pain in the right lower quadrant, which had reappeared at intervals of days and lasted only a few minutes each time. The same symptoms were found as in the first case, but the tumefaction, although slightly movable transversally, was absolutely immovable longitudinally. Median subumbilical laparotomy disclosed a hematoma and the patient was soon discharged as

cured. In this case also, the hematoma was ascribed to injury of an epigastric vessel.

Deep chronic phlegmon of the abdominal wall is often mistaken for a malignant tumor because usually there is nearly complete absence of fever, the patient's general condition is bad, the course of the disorder is protracted, and the physical signs are deceptive. Generally, the morbid process originates in the lymph nodes which accompany the epigastric vessels in the suprapubic space, or in the deeper lymph nodes of the prevesical space of Retzius; but phlegmon may develop also in the properitoneal connective tissue which, through peritoneal adhesions, may be in contact with infected abdominal viscera. A case in point is that of a man who was admitted with the diagnosis of malignant abdominal tumor of rather rapid course, in whom a suprapubic hard mass extended laterally toward the inguinal arches. The mass was almost painless, nonadherent to the skin, and immovable. The patient had no fever and was in a debilitated condition These symptoms and a gonorrheal history of 20 years raised the suspicion of chronic phlegmon, which was confirmed by puncture

Roentgenographic Symptoms in Abdominal Injuries—According to H. Laurell⁵ roentgenography seems to be used but little as an aid in the determination of the nature of injuries of the viscera due to external dull force directed against the abdomen The literature mentions mostly only the possibility of confirming the presence of free gas in the abdomen as an expression of perforation of gas-containing organs. The diagnostic value of intravenous and retrograde urography in rupture of the renal pelvis and other portions of the urinary tract is also mentioned. It is

usually forgotten that free fluid in the abdomen can be demonstrated roent-genographically, often much earlier and more definitely than with ordinary clin-cal examination. This is true also of inflammatory exudate, pus, transudate, and hemorrhage. It is also forgotten that retroperitoneal hemorrhages and infiltrations show roentgenographic symptoms similar to those of paranephritis.

The author shows the diagnostic value of roentgenography in 30 cases of subcutaneous abdominal injuries, including mainly ruptures of the kidney, liver, spleen, or intestine, and also abdominal contusions with renal hemorrhage and other internal injuries. With subcutaneous abdominal injuries the life-threatening hemorrhage or beginning peritonitis demand early diagnosis and surgical intervention, as in the presence of these complications the prognosis becomes worse with every hour of delay. Unfortunately, the early diagnosis is seriously hampered by shock, which may last 3 hours. Often the patient is seen only after the shock has passed If the symptoms of internal hemorrhage or peritonitis are then pronounced, the operation is usually done without previous roentgenography. This is also done when the complications are evident in spite of existing shock. Many surgeons claim that the operations should be avoided during shock when the diagnosis is uncertain, and should be done after the shock has worn off, when hemorrhage or peritonitis is present. Others believe that an exploratory operation, whether shock is present or not, should be done as soon as there is the slightest suspicion of these complications viewpoint is based not only upon the experience that an exploratory laparotomy is a relatively harmless intervention and that the prognosis is much better with early operation, but also upon the fact that the clinical signs of free fluid or free gas in the abdomen following rupture or perforation often appear relatively late and even then may be quite uncertain. They often become positive only after the free gas or fluid is abundant.

Following the rupture of abdominal viscera, the contents and blood often enter the free abdominal cavity. The free fluid also increases from the ınflammation and exudation of the peritoneum caused by the contents of the digestive tract, urine, bile, and blood As free fluid in the abdomen is an early and important symptom of visceral injury, but often is clinically demonstrable only late, other diagnostic aids, such as exploratory puncture, have been suggested, but some surgeons object to this because of the danger of intestinal injuries. The clinical symptom of free fluid, displaceable dullness in the loin, may also occur in ileus of the small intestine with fluid in the gut Here again an exploratory puncture may be dangerous, as well as when the free fluid in the abdomen is present in a small amount or only in certain places

Hence it must be considered as progress that the presence of free fluid in the abdomen can be demonstrated with the harmless method of roentgenography, especially when the fluid is present in such a small amount that the clinical examination gives only uncertain or negative findings. With beginning peritoritis following perforation of the digestive tract, the clinical picture (muscle defense) is often diagnostically decisive long before the free fluid is clinically demonstrable. In such cases, roentgenography is a valuable aid

The Syndrome of Abdominothoracic Lesions

The knowledge of the abdominothoracic syndrome is of great importance for every surgeon because many pathological conditions of the thoracic organs may

simulate surgical diseases of the abdomen and vice versa. L. Moncalvi⁶ points out that either the pathological process may spread by contiguity, or certain reflexes may be responsible for the confusion because numerous anastomoses between the cerebrospinal and the sympathetic system offer infinite possibilities of various combinations of symptoms.

sounds over the thorax, abdominal pains, digestive disturbances, and vomiting. A roentgenographic examination after an opaque meal or pneumoperitoneum is essential.

A subphrenic abscess may produce intercostal pains, dyspnea, an abnormal distention of one-half of the chest, and dullness on percussion, as well as vomit-



Fig 1—Batson's dissection to show the nerve supply and the sheath of the rectus muscle. The continuation of the fleshy fibers of the transversus abdominus muscle behind the aponeurotic sheath is shown. In a less well muscled individual, these appear as a fascial plane, (Hartzell and Winfield Surg, Gynec and Obst.)

Traumas may involve the thorax and the abdomen, causing on the one hand subcutaneous emphysema, hemopneumothorax, and hemopericardium, and on the other hand pains in the abdomen, hemoperitoneum, pneumoperitoneum, and hematuria. An exploratory laparotomy should be followed by an aspiration of the hemothorax

A congenital or acquired spontaneous or traumatic hernia may produce dyspnea, borborygmi, abnormal percussion

ing, meteorism, and descent of the lower hepatic border

In addition to the well-known abdominal symptoms, such as pain in the epigastrium and tympanites, a perforation of a gastric or duodenal ulcer may cause thoracic signs, viz., cyanosis, tachycardia, dyspnea, and limitation of respiratory movements

Inflammation of a subhepatic or retrocolic appendix may produce, in addition to pains in the right upper quadrant of

the abdomen, pains in the chest, limitation of the respiratory movements, and dullness over the base of the right lung. A concomitant pneumonic focus, a bronchopleural involvement, or a valvular endocarditis in the course of a peritonitis should not be overlooked. Vague abdomnal pains combined with right, left, or

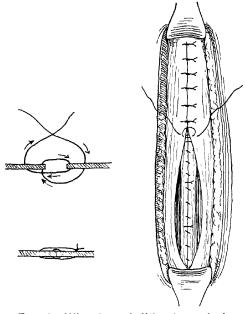


Fig 2—Whipple and Elliott's method of fine-silk closure of a clean abdominal incision. The peritoneum is closed with a continuous fine-silk suture, and is then temforced every 2 cm with interrupted silk sutures. The fascia is then closed with the "far and near" stitch (Haitzell and Winfield Surg., Gynec and Obst.)

bilateral serous pleurisy or pericarditis suggest *polyserositis*, for which pericardiolysis or cardio-omentopexy may be considered

Among chest conditions responsible for an abdominal symptomatology, pneumonia and basal, diaphragmatic, or mediastinal pleurisy must be mentioned. In addition to the typical signs they may cause acute pains in the epigastrium or hypochondrium and vomiting, thus simulating an appendicitis. Furthermore, angina pectoris, caused by an aortitis or a coronary sclerosis, may lead to an arrhythmia, tachycardia, dyspnea, and

cyanosis in addition to sharp epigastric pains, vomiting, and other abdominal symptoms.

Disruption of Abdominal Wounds

From a study of the literature on wound disruption certain points appear of importance.

The reported incidence of wound disruption averages 1.5 per cent, with a mortality of 35 per cent. The age, sex, and race of the patient are unimportant factors. Seasonal variation may have some bearing, insofar as it predisposes to respiratory infections.

The general condition of the patient and the underlying disease for which the operation is performed must be considered as important predisposing factors. Obesity, anemia, and concurrent systemic disease may affect the progress of wound healing. In addition, there are certain less obvious factors attributable to the patient which influence wound healing. These are vitamin C deficiency, hypoproteinemia, and catgut allergy.

Consensus would indicate that wound disruption is essentially a complication of the vertical incision. J. B. Hartzell and J. M. Winfield? cannot definitely say whether the lower or upper abdominal wound is more prone to disrupt. They believe that any incision which seriously impairs the blood and nerve supply of the abdominal musculature is more prone to separate, and also that it is more difficult to secure and maintain an accurate approximation of the transversalis fascia when its fibers are cut across.

The authors refer mainly to those vertical incisions which split or lie lateral to the rectus muscle. They believe that the preponderance of evidence is against the use of the vertical abdominal incisions, and urge a wider use of the transverse, oblique-muscle, and fascia-splitting incisions whenever possible.

The authors believe, with the majority of writers, that no method of closure or type of suture is proof against wound disruption. In clean cases, the fine silk closure, as described by Whipple, would seem to be ideal. In infected cases, the use of a fine chromic catgut with the "silk technic" is probably as good as any procedure. The value of nonabsorbable tension sutures is under considerable discussion at the present time. Those

Drainage through the incision probably favors disruption. It would seem logical to use a stab wound some distance from the incision when possible. If drainage of the incision is considered necessary, the peritoneum should be closed and a drain placed down to it.

With but few exceptions, practically every writer believes that a stormy postoperative course, complicated by coughing, hiccough, vomiting, distention, and



Fig 3—Horner advises the use of an efficient abdominal support in the form of an adhesive corset. The one illustrated permits of frequent inspection of the incision (Hartzell and Winfield Surg , Gynec and Obst)

who favor these sutures believe that they take the strain off the suture line, and make for a stronger closure. Those against their use believe that they strangulate tissue, tend to cut through, cause local necrosis, and often result in small stitch abscesses and wound infection.

The through-and-through method of closure with silver or steel wire has many adherents and is undoubtedly an excellent method of closure in infected cases and in those cases in which at the time of closure there is a possibility of disruption. The authors also believe that there is an additional factor of safety in the application of a good abdominal support.

undue restlessness, resulting in increased abdominal pressure, predisposes to disruption

Infection may be considered a contributing factor in wound disruption

A sharp pain in the vicinity of the incision or a feeling of something "giving way" during a fit of coughing or vomiting may mean a disruption has occurred A knuckle of bowel may protrude into the deep layers of the incision and become partially obstructed, which results in an increasing degree of vomiting and distention () from the only sign may be serosangumous drainage on the dressings.

The most dangerous period is from the fifth to the tenth day.

Following a disruption, it is important that a closure be effected as soon as possible. Immediate resuture is the method of choice in those clean cases in which the patients are not particularly ill. It would seem that some type of nonirritating through-and-through suture, such as steel wire, is preferable. The sutures should be closely spaced, in order to

carefully approximate the peritoneum. In infected cases, or in those individuals who are gravely ill, strapping the wound with flamed adhesive tape over a gauze pack is preferable to immediate resuture.

It is impossible to estimate accurately the effect of disruption upon the mortality. Our impression would be that from one-third to one-half of the deaths occur-

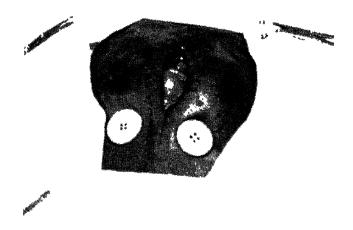


Fig 4—Disciption of an abdominal wound with evisceration, occurring in a 68-year-old male negro. The patient was thin and undernourished, but seemed to be in fair general condition. He had been suffering from severe intermittent abdominal pain for 48 hours prior to admission to the hospital, and a diagnosis of volvulus was made. The abdomen was opened through a mid-left paramedian incision, and a large distended volvulus of the sigmoid was encountered and was easily released. A rectal tube was inserted, and following this marked deflation of the large bowel occurred promptly.

The abdomen was closed with a continuous fine silk suture in the peritoneum and posterior tascia, interrupted silk sutures in the fascia, and 3 fine steel-wire tension sutures including the anterior rectus fascia. The skin was closed with clips. The postoperative course was uneventful A rectal tube and gastric suction tube were inserted. There was no distention or vomiting. The nasal and rectal tubes were removed on the third postoperative day, and from then on the temperature did not mount above 100. It and the pulse ranged between 70 and 80.

On the seventh postoperative day the wound was inspected. It appeared a little swollen, and it was noticed that the middle tension suture had broken. There was some bloody fluid on the dressing, and following the removal of the skin clips about 2 ft of small bowel mimediately eviscerated. The intestines were reinserted, the wound strapped, and the patient taken to the operating room. Under local novocam infiltration, a secondary closure was performed using closely placed through-and-through stainless steel-wire sutures.

Inspection of the wound revealed it to be clean, and the margins glistening and free of exudate or granulations, without any evidence of healing. The silk stitches had cut through the tissues

Immediately following the secondary closure, the serum-protein determination showed 5 6 per cent total. The albumin-globulin ratio was 1 24 (normal total serum-protein determinations average about 7 1 per cent, and the albumin-globulin ratio is normally about 1 53) The ascorbic-acid determination, by the method of Pijoan and Klempeier, showed 0 13 mg of ascorbic acid per 100 cc of blood plasma (normals reported by their method lange between 0.65 to 2 mg per 100 cc of blood plasma)

The patient was given a transfusion of 500 cc of citrated blood and cevitamic acid. His convalescence following secondary closure was uneventful (Hartzell and Winfield. Surg., Gynec and Obst.)

ring shortly after a disruption may be directly attributable to disruption. Peritonitis is the actual cause of death in many instances.

Why does the disrupted wound, secondarily closed, often heal so promptly? This is a difficult question, and so far as the authors know, has not been positively answered. Recurrences have been reported, but they are rare. The healing of an infected wound which disrupts seems to need but little discussion. As the infection cleans up, the wound heals by granulation. However, the clean wound which separates without apparent cause and heals rapidly on resuture offers a more difficult problem. Possibly the transfusion, so frequently administered following the secondary closure, may be Possibly the actual trauma a factor which occurs at the time of the separation and the resuture may afford sufficient stimulation to promote healing

In attempting to outline a prophylactic régime for the prevention of wound disruption, many of the casual and predisposing factors must be given serious consideration. For the sake of brevity, the authors have listed below those that seem most important to them

- 1 Adequate preoperative preparation when possible, a diet rich in vitamin C, and blood transfusions if indicated
- 2. The wider use of more anatomical incisions, preservation of the nerve and blood supply, and avoidance, when possible, of the vertical incision through the tendinous attachment of the internal oblique and transversalis muscles
 - 3 Meticulous surgical technic
- 4 An accurate approximation of all layers of the incision, especially the peritoneal layer.
- 5 Avoidance of the use of catgut, and the wider use of silk in clean cases
- 6 Avoidance of dramage through the incision
- 7. A satisfactory anesthesia, giving good relaxation.

- 8. The use of duodenal suction and small intestinal intubation to combat vomiting and distention.
- 9. The general use of an effective abdominal support.

DUODENUM

Diverticulum of the Duodenum

Diverticula of the duodenum are classified as primary and secondary. A primary diverticulum is one which occurs without any obvious cause; its wall is formed by the mucosal and submucosal coats. These diverticula are found in the second, third, and fourth portions of the duodenum. Secondary diverticula are considered as having an obvious cause These are found in the first part of the duodenum and their walls are made up of all the coats of the intestine

Table 1 as presented by D. Wheeler⁸ shows the incidence of duodenal diverticulum as found by several workers on cadaver or post-mortem material.

Table 2 indicates the frequency of the condition discovered by roentgen examination

Secondary diverticula occur in the first part of the duodenum and are the result of scarring and contraction due to an ulcer with pouch formation, this pouch being the diverticulum. This obstruction of the duodenal cap, which is due to scarring, causes a stenosis, and if the obstruction is of sufficient severity the proximal portion of the cap will dilate This type of diverticulum will have all the coats of the bowel remaining in its wall Since the diverticulum is the result of an underlying condition, e^{-g} , ulcer, it gives no sympoms. Most patients have, therefore, been treated by operation designed to cure the primary trouble

Primary diverticula have the following characteristics: (1) They are found only

TABLE 1—Percentage of All Types of Diverticula Found Post-Mortem

Author	Post- Mortems	Cases of Divertic- ulosis	Per- cent- age
Linsmayer	1367	45	3.3
Baldwin	105	15	14.2
Grant	37 (cadaver)	6	16.0
Grant	133 (cadaver)	15	11.3

(Wheeler: Canad. M. A. J.)

in the second, third, and fourth parts of the duodenum, the most frequent site being the second portion; (2) they are found on the inside of the duodenal loop and are, therefore, in relationship to the head of the pancreas; (3) they are often multiple, when they are usually seen as goblet-shaped protrusions of the mucous membrane communicating with the lumen of the duodenum by a narrow neck; (4) they vary in size, from that of a small pea to that of a small walnut; and (5) they are more frequently seen after the fifth decade

There are no definite signs or symptoms which are pathognomonic of these pouches. The history is usually of long standing. The patient complains of a feeling of heaviness and distention after eating, perhaps of nausea and voniting, and sometimes diarrhea. The only method of diagnosis of these pouches is by use of the barium meal.

The author agrees with Odger's statement that "the great majority of these pouches does not cause any trouble, and since their demonstration by x-rays, their significance has probably been exaggerated." Maclean, however, maintains that in those cases in which there is a definite peridiverticulitis and pancreatitis from the embedding of these pouches in that gland, surgical removal offers definite promise of relief. However, it is customary to try medical treatment first, such as postural drainage and lubrica-

TABLE 2

Author	Cases Examined	Cases Diagnosed as Diverticulosis	Per- cent- age
Case . Andrews Spriggs and Marxer . Cryderman J. C McMillan (quoted by	6847 2200	85 26	1 2 0 18
	1000 770	38 40	3 8 5 19
Maclean)	653	10	1.5

(Wheeler: Canad M A J)

tion and disinfection of the diverticular pouch.

A case of perforated duodenal diverticulum is presented by F. K. Boland, Jr.9 The symptoms and signs are similar to those of a perforated peptic ulcer The diagnosis may be missed, as it was in this patient, unless the possibility of such a condition is kept in mind. The author would suggest that if the signs and symptoms point to a perforated ulcer and the intraperitoneal pathology reveals nothing more than an exudate along the anterior duodenal wall a small incision be made in the posterior peritoneum and a search begun for a diverticulum

Duodenal Ulcer

The surgical physiology of duodenal ulcer is explained by V. G. Burden 10 He believes that many of the clinical features of duodenal ulcer can be explained by the activity of the pyloric spluncter. It may cause the typical symptoms of ulcer when no ulcer is present, since the ulcer itself does not cause the symptoms which identify its presence Dysfunction of the pyloric sphincter is one and hyperacidity is the other main factor in the etiology of duodenal ulcer. The normal stomach regulates its own acidity. Failure of this control means the development and maintenance of a duodenal ulcer The pyloric sphincter because of spasm or failure to relax becomes a potent hindrance to the regurgitation of alkaline duodenal contents into the stomach. Of the 2 factors concerned in the etiology and maintenance of duodenal ulcer, dysfunction of the pyloric sphincter alone is amenable to direct attack. Its function can be abolished permanently by removing the anterior half

averaged 14,000. Of these, approximately 12,000 are engaged in executive or clerical work, and 2000 are employed in the Commissary, Building and Printing Departments. Ages of the personnel range from 18 to 70 years. The ratio of women to men is roughly $2\frac{1}{2}$ to 1. Although perhaps not representative of the whole population of this section of the Country,

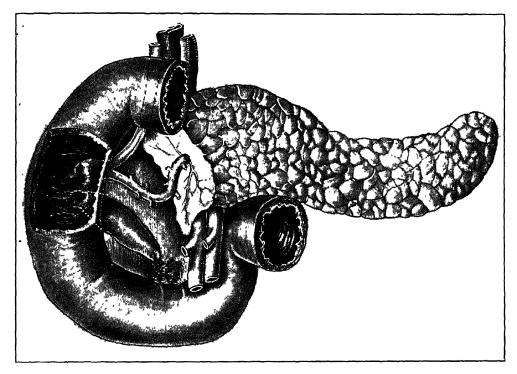


Fig 5—A diagrammatic sketch showing a perforated duodenal diverticulum. The head of the pancreas was omitted from drawing and a small window was made in the anterior wall of the duodenum to demonstrate the diverticulum and its perforation at the tip (F K Boland, Jr.: Surgery)

of the sphincter without opening into the duodenum or stomach. This procedure has been carried out with lasting success in cases of duodenal ulcer.

Incidence of Ulcer and Results of Treatment—An analysis of the cases of duodenal ulcer diagnosed and observed at the Home Office of the Metropolitan Life Insurance Company from the year 1927 through the year 1936, has been studied by J. Jennison. All patients came from the personnel of the Home Office, which during the above period

this group offers variety as to age, occupation, and race. (In the average, they belong to the group of the economic population which consults general practitioners rather than clinics or specialists.

The analysis of this particular group of employees with chronic recurring duodenal ulcer is of value because of the opportunity for a complete follow-up in the majority of cases.

Correct diagnosis, together with conservative medical treatment, has kept most of the group comfortable. Unsatis-

factory results were frequently due to inadequate management.

The incidence of chronic recurring duodenal ulcer in the entire personnel is at least 1.38 per cent, and is in all probability about 2 per cent. Among the employees over age 30, the incidence of diagnosed cases is 2.4 per cent.

The small percentage of cases which had complications was responsible for a substantial loss of time from work. Severe complications have been relatively rare. Hemorrhage, the most frequent complication, occurred almost equally in all decades from the third through the sixth, and was responsible for half of the total days lost from work.

The building group, representing skilled and unskilled laborers, showed the highest absence record, 39 per cent of the total for the entire group. Time lost from work because of chronic duodenal ulcer represents less than 05 per cent of the total number of days lost by all employees for all causes during the same period.

Gastroduodenostomy for Certain Duodenal Ulcers—The technic of gastroduodenostomy and results obtained therefrom have been described by H. M. Clute and J. S. Sprague 12. The procedure appears more physiological because it empties the gastric content into the duodenum rather than into the jejunum However, they found that 5 of their patients, after a gastroduodenostomy, had total and free acids which were nearly as high as, or higher than they had been before operation This observation was surprising to them because all of the patients were clinically well, and recent x-ray studies showed no evidence of pathological changes After reviewing the literature, the conclusion is drawn that "only 3 stomal ulcers (have occurred) after nearly 400 operations, an incidence of less than 1 per cent." This is contrasted with the 8.5 per cent of stomal ulcers reported by Wright, of England, in his careful collective inqury of 1935. The fact is noted, however, that Graham reported 1 stomal ulcer in 9 gastroduodenostomies done by him.

In the authors' experience, gastroduodenostomy has been satisfactory in relieving pyloric stenosis. It has been used in the cases of 7 patients during the past 3½ years Four of these patients were in a serious condition when first treated. The postoperative course of these patients was surprisingly comfortable. This same procedure was used in the cases of 2 additional patients who had persistent pain in duodenal ulcers despite long medical treatment. They have both been well for 1 and 2 years, respectively, but, to date, show high values for total acidity. Because of the persistent postoperative high gastric acidity, Clute and Sprague have hesitated in using the operation for nonobstructed duodenal ulcer in patients in whom medical management has failed, and they believe that they would be more optimistic about the future of the 2 last mentioned patients if a subtotal gastrectomy had been done

The same surgical procedure has been used in patients with duodenal ulcer, who have had massive gastric hemorrhage. Although the procedure is not ideal for this complication, it permits exposure and suture of the bleeding vessel in the base of the duodenal ulcer, and it is indicated for certain bleeding ulcers in patients who are in poor condition. In addition, the operation has been used with resection of an ulcer situated very high on the lesser curvature of the stomach, but the routine use of this operation for ulcers of the lesser curvature is not recommended.

Gastroduodenostomy has also been particularly helpful in the successful management of 2 bleeding gastrojejunal ul-

cers, in which it was possible to remove the jejunum from the stomach, remove the ulcer from the jejunal wall, close the jejunum, and overcome the pyloric obstruction. The ideal procedure at the present time in patients of this type, *i. e.*, gastric resection, occasionally proves to be too much in the way of surgical intervention. For this reason, gastroduodenostomy is substituted for gastric resection.

Carcinoma of Duodenum

A clinical and pathologic review of carcinoma of the peripapillary region of the duodenum, based on 17 new cases and 205 cases reported in the literature has been presented by M. M. Lieber, et al. 13 Thirteen of the authors' cases and one from the literature were found in 22,152 necropsies and 3 in 4154 necropsies. The average age was about 54.4 years Eighty-three of the patients were women and 139 were men. Only 13 cases occurred in individuals from 15 to 34 years of age. The onset was acute in about 80 and gradual in 20 per cent of the cases.

The principal symptoms and signs, irrespective of the mode of onset, were jaundice, pain, loss of weight and strength, anorexia, fever, vomiting, constipation, diarrhea, and a sense of weight and pressure in the abdomen. Other less common symptoms were dyspepsia, epigastric distress, flatulence, abdominal distention, nausea, and chills Jaundice was a symptom in 98 2 per cent of the cases and pain in 594 per cent; both were associated at the onset of the condition in 243 per cent. Fever, sometimes accompanied by chills, occurred in 33 3 per cent of cases, usually late in the condition. A mass was palpable clinically in the region of the primary tumor in only 4 cases The liver was palpably enlarged in 77.9 per cent of cases and the gall-bladder in 499 per

cent. A moderate grade of anemia was the rule in these patients.

A correct preoperative diagnosis was made in approximately 17.1 per cent of cases. The presence of a lesion in the region of the papilla of Vater was recognized roentgenographically in 16 of 60 cases examined. At celiotomy, a correct surgical diagnosis was made in approximately 68 per cent of 122 cases. Ninety-seven of 100 patients, treated medically and not subjected to surgery, died on an average of 6.63 months after the onset of the illness.

Surgical therapy was instituted in 122 cases. There was an ultimate mortality rate of 72 per cent. The operative mortality was 50.6 per cent. Of 51 patients subjected only to some type of palliative procedure for the relief of obstructive jaundice, the operative mortality was 78.4 per cent. Of 57 patients in whom the primary growth was resected either alone or in combination with other surgical procedures, the operative mortality was 30 per cent. The patients who died immediately after an operation were ill for an average of 6 months before operation Other patients who were operated on and who survived the immediate postoperative effects lived for an average of 2 years after the onset of the condition, and a little more than one-half of these were reported alive at the end of this period; of this group, those who died were ill for an average of 7 months before operation, whereas those reported as still living were ill for an average of only 2 months after operation. These figures emphasize the importance of early diagnosis and early surgical treatment

BILIARY TRACT AND LIVER

Roentgen Diagnosis of Surgical Diseases of the Liver and Biliary Tract—Roentgen examination may be

valuable in the demonstration of many lesions involving the liver. It may show (1) variations in density, such as calcification, gas shadows, fluid levels, opaque media; and (2) variations in size, shape, or position of the liver itself, or of its neighboring organs, visualized with or without opaque media.

E. P. Pendergrass and G. W. Chamberlin¹⁴ show that calcification in the liver is not common When present, it is seen more often in centrally necrosed lobules, but it has been observed in Glisson's capsule, in cases of nephritis. It may occur as a result of small abscesses, thrombosis associated with cavernous angiomas of the liver, and perihepatitis. Occasionally, if roentgenograms are made of patients in the erect posture, air and fluid levels in the liver can be shown; they indicate abscess or cyst. The roentgen criteria of liver abscess are elevation of the diaphragm, restriction of motion of the diaphragm, and a more or less hazy increase in density involving the lower right lung field. An abscess of the left lobe of the liver is less likely to affect the diaphragm

Thorum dioxide sol has been used in the demonstration of diseases of the liver When injected intravenously, it causes increased density of the liver and spleen Hepatosplenography has been utilized (1) to determine the nature of a mass in the upper part of the abdomen, (2) to determine the presence and kind of hepatic disease, such as atrophic cirrhosis, hypertrophic cirrhosis, syphilis, metastatic lesions, present in the liver, if operation for carcinoma is contemplated; (3) to demonstrate rupture of the liver or spleen; (4) to determine the cause of jaundice whether it is intrahepatic or is due to obstruction of the common bile duct; (5) to follow the progress of hepatic or splenic disease; (6) to demonstrate whether a lesion is above or below the

diaphragm; (7) to diagnose ascites; and (8) to study diseases of the spleen.

The normal liver is not a fixed organ but, within certain limits, it is freely movable in the abdominal cavity. Buerger has observed 2 cases of partial dystopia of the liver, in which there was an interposition of portions of the intestinal tract between the liver and the diaphragm, or lateral abdominal wall. Distention of these loops by gas may cause pain which may radiate to the back and to the right shoulder. Complete situs transversus is not difficult of diagnosis. Riedel's lobe may be readily demonstrable in the properly exposed roentgenogram, while anomalies in size of the liver may occur as a diminution in the right or left lobe, or as an increase in the size of any of the 4 lobes.

The nomenclature and interpretation of roentgenograms of the gall-bladder following the administration of dye are as follows

- A Functioning gall-bladder This includes gall-bladders which showed good concentration of the dve and good emptying after the fatty meal. Sub-classification is based on the presence of stones, mural growth, adhesions, or anomalies.
- B Partially functioning gall-bladder In this type there is inadequate concentration of the dye or mability to empty properly. Sub-classification is based on the presence of stones or anomalies
- C Abnormally functioning gall-bladder. These gall-bladders are poorly visualized, or not visualized at all, or they increase in size during the examination, and reflux is indicated. Subclassification is based on the presence of opaque or non-opaque stones, milk of calcium bile, calcified gall-bladder, and anomalies.

The commonest opaque shadows in the right upper abdomen which may be confused with gall-stones are renal calculi, calcified glands or vessels, barium in diverticuli of the colon, calcification in the liver or pancreas, and calcification of a tuberculous absess Repeated exammations in various postures are frequently necessary for proper interpretation. Pyelography may be necessary to exclude renal pathology.

Milk of calcium is chiefly calcium carbonate in the gall-bladder. The roentgenogram shows a dense gall-bladder shadow. The organ itself is sometimes shrunken and does not empty after the fatty meal. Tumors may be suspected upon the finding of one (or more) clear oval or circular defect which remains constant with changes in the position of the patient.

Anomalies of the shape and position of the gall-bladder are detected by cholecystography

The demonstration of stones in the common duct during operation by the injection of an opaque medium with immediate x-ray examination is a recent accomplishment. Delayed examination of the common duct by the injection of a radio-opaque substance through a T-tube is of value in the determination of the condition of the common duct.

Liver Abscess

The late results in the treatment of amebic abscess of the liver have been studied by P W. Brown and C H. Hodgson 15 Thirty-five cases (18 surgical and 17 medical) of abscess of the liver were encountered during a period of 18 years at the Mayo Clinic results of their study show that the infection occurs most frequently in middle-aged male patients. A syndrome of pain in the upper right quadrant of the abdomen, often referred to the shoulder, associated with fever, chills, leukocytosis, and possibly with diarrhea and jaundice, should suggest hepatic involvement and, if relieved by antiamebic treatment, should be an indication of amebic infection.

The authors believe that the efficacy of the antiamebic treatment can be meassured partially by the remarkable results obtained in their relatively small series of 35 cases. A follow-up study of the late results in these cases revealed that 12 of the 14 medical patients, and 14 of the 18 surgical patients are apparently well at the present time. The nucleus of their treatment of this dreaded infection lies in their slogan: "Emetine to check the acute symptoms and arsenic to wipe out the amebas." They contend that the employment of this method is desirable as well as justifiable until another method which is just as effective and causes less toxicity is made available.

Primary Carcinoma of Liver

Primary carcinoma of the liver is a fairly rare disease as compared with secondary growths. The dictum of Virchow, "Such organs as are the frequent sites of secondary tumors rarely exhibit the primary type," still can be applied to the liver.

In reviewing the obtainable literature of the last 10 years, J. M. Greene¹⁶ was able to collect 386 post-mortem or biopsied cases.

Primary carcinoma of the liver does not exempt any age. It may be found in very young children, although rarely, and, as reported by Mueller, in a patient 83 years old The youngest case was reported by Stiner, a primary carcinoma in a male of 4 months. The finding of primary carcinoma of the liver in the very young has led some observers to believe perhaps these tumors arise from embryonic rests

In reviewing the literature there were found 75 proved cases in children up to 16 years of age. It was found that 532 per cent of the carcinomas occurred in infants under the age of 2 years, 68 per cent of whom were males, while 32 per cent were females.

Etiology — Many different factors have been cited as causes of primary car-

cinoma of the liver. The true cause is still unknown just as the cause of carcinoma elsewhere in the body is unknown. As many observers believe that irritation is one of the factors in carcinoma elsewhere in the body, so it is believed that previous hepatic disease predisposes to primary carcinoma of the liver. Syphilis, malaria, alcoholism, cirrhosis, trauma, parasitic infections, and other causes have been accused of being the causative factors in the development of this condition

By far, cirrhosis of the liver is looked upon, by most observers, as the chief causative factor of primary carcinoma of the liver. From 75 to 100 per cent of all hepatomas are associated with cirrhosis and approximately 50 per cent of all cholangiomas are associated with cirrhosis (Yamagiwa). Jaffe was of the opinion that 90 per cent of all primary carcinomas of the liver were associated with cirrhosis. Strong and Pitts state, "It is our impression that primary carcinoma of the liver invariably develops on a basis of cirrhosis." Ewing believes that the tumor process appears to be the direct sequel of, or is essentially connected with cirrhosis Primary carcinoma of the liver almost never occurs without a preceding cirrhosis (Mallory) It was found, in this review, that 87 per cent of the hepatomas and 37 per cent of the cholangiomas were associated with cirrhosis. These figures fall in closely with those observed by others

Pathology—Histologically, Ewing is of the opinion that hepatomas can be traced to hypertrophic liver cords, and that there is a uniform gradation between nodular hyperplasia, multiple adenoma, and multiple carcinoma; also that cholangiomas have been traced satisfactorily to the proliferating bile ducts in cirrhotic and other types of livers

For the atypical and highly malignant growths from both sources, there are no

observations to indicate their original origin.

It is an interesting fact that metastasis from primary carcinoma of the liver is much less frequent than from carcinoma elsewhere in the body. Intrahepatic spread is by far the most common. Fox and Bartels compiled 80 cases and showed that in 40 per cent there were metastases and that in 263 per cent the metastases were in the lungs. Hill is of the opinion that metastases are comparatively rare and states that usually there is portal or hepatic invasion with extension even along the inferior vena cava into the right auricle of the heart. It has also been shown that if metastases do occur they are found in the regional nodes, lungs, and spleen. Hepatomas metastasize more often than cholangiomas (Ewing).

Symptoms and Diagnosis—The clinical features, symptoms, and diagnosis of primary carcinoma of the liver differ in every case. A review of the literature shows definitely that there is no clinical course which characterizes this disease. The diagnosis in the vast majority of the cases is made at autopsy.

The symptoms are most misleading and almost any symptom may manifest itself. At times there may be vague gastrointestinal symptoms with variable physical findings. One feature which is believed to be rather common is the early fixation of the liver with the tendency toward enlargement upward more often than downward, because of the fact that there is less resistance offered by the diaphragm and lung than by the fluidfilled peritoneal cavity (Strong and Pitts). Because of this type of enlargement the liver is often not found or overlooked as there is little or no extension below the costal margin.

Ewing divides the clinical cases into 4 groups. The first is that group in which there are no symptoms and death occurs

from hemorrhage within a few days after the onset. The second group consists of those patients who have died with a diagnosis of cirrhosis of the liver. In the third group we find those cases in which there has been a history of cirrhosis, jaundice, ascites, cachexia, and the finding of a tumor mass in the liver. In the fourth group are placed those patients who develop a carcinoma of the liver although they were healthy previously.

In this series the most constant and frequent finding was ascites. This was present in 66 per cent of the cases, the amount of ascites varying from an amount which caused but a slight increase in the size of the abdomen to amounts so large that the liver could not be palpated until a paracentesis had been done These findings fit in well when we note that 49 per cent of all cases of primary carcinoma had an accompanying cirrhosis The ascites is apparently on an obstructive basis.

Treatment—The duration of the disease is slow. Although rare, ante-mortem diagnosis of primary carcinoma of the liver has been made. In some of these cases lobectomies were attempted but without much success. The longest cure was 6 months

Surgical Aspects of Hypoglycemia Associated With Damage to the Liver

One of the many important functions of the liver is concerned with carbohydrate metabolism. It is fairly well established that the liver makes and stores glycogen and liberates it to the blood stream as dextrose, through which mechanism the normal glycemic level is maintained. It has been shown that gross interference with the liver, such as surgical extirpation, massive destruction by poisoning or replacement of large amounts.

of liver tissue by tumor, greatly disturbs this function.

F. A. Coller and H. C. Jackson¹⁷ cite cases as examples of severe and moderately severe hypoglycemia. The patients presented chronic cholecystic disease associated with cholelithiasis; the first had severe involvement and the others milder involvement. Biopsy revealed accompanying inflammatory changes in the liver parenchyma in each case. Dextrose tolerance tests were performed in each instance before and after operation. Dextrose tolerance curves made before operation showed variations from normal which indicated damage to the liver as judged by the criteria of Coller and Troost. Studies after operation showed a return toward normal. In none of the cases was there any abnormality of the pancreas which could be determined at operation. In the first 2 cases, studies with the respiration chamber were carried out before operation, as reported elsewhere by Conn and Newburgh, showing that carbohydrate was oxidized normally and thus disproving the possibility of oversecretion of insulin. All 3 patients had symptoms caused by hypoglycemia which were modified by removal of the gall-bladder.

Regardless of the exact physiologic and biochemical processes, these cases are interesting since they illustrate a cause of hypoglycemia quite definitely not due to oversecretion of insulin They illustrate another of the possible complications of chronic disease of the gallbladder and bile ducts and demonstrate that carbohydrate metabolism may be seriously disturbed by the accompanying hepatitis and cholangiolitis The fact that such disturbances may occur is another reason for urging early operation on the diseased gall-bladder, especially since the return of carbohydrate metab-

olism to normal may be slow and perhaps never complete.

Also the authors believe that these cases are important since they call to mind a cause of spontaneous hypoglycemic states as yet unconsidered. The liver disease was definite but not as destructive as has been present in previously reported cases of hepatic hypoglycemia. The authors believe that chronic cholecystitis and cholelithiasis with the accompanying changes in the liver must be added to the causes of extrapancreatic hypoglycemia.

Coller and Jackson summarize by stating that hypoglycemia is a definite clinical state which in its more severe degrees has usually been assigned to hyperinsulinism

The liver plays an important part in carbohydrate metabolism, and there is indubitable evidence that severe damage to the liver may cause hypoglycemia

Cholesterol Metabolism and Biliary Tract Disease

Disturbances of the cholesterol metabolism, although generally conceded to be a major contributing cause in the formation of gall-stones, are as yet little understood Cholesterol is both exogenous and endogenous in source. Because of the partial exogenous source, the dietary treatment of disease of the biliary tract associated with hypercholesteremia is based on a 2-fold hypothesis (a) That hypercholesteremia may result from the excessive ingestion of foods which are high in cholesterol and fat content, and (b) that a reduction of cholesterol intake by patients having hypercholesteremia causes a decrease in the amount of cholesterol in the blood It may be stated that a relative increase in the cholesterol concentration of the gall-bladder bile, particularly in the presence of infection

or stasis, may result in the precipitation of cholesterol and the formation of stones.

- J. R. Twiss and J. H. Barnard¹⁸ investigated a series of patients with disease of the biliary tract and hypercholesteremia. All patients with jaundice or obstruction of the common duct were eliminated by the exclusion of those in whom the icterus index was elevated. The studies may be summarized as follows.
- 1 A series of 110 medical and surgical patients with disease of the gall-bladder and associated hypercholesteremia was placed on a low cholesterol diet. A control series of 35 patients did not receive this diet.
- 2 Of 80 medical patients 82 per cent showed an appreciable reduction in the blood cholesterol, 80 per cent were symptomatically benefited. Fifty per cent of the control group showed an inconsequential reduction of the blood cholesterol; 33 per cent were symptomatically benefited.
- 3 Sixty-seven per cent of the 30 surgical patients placed on the low cholesterol diet after cholecystectomy showed an average reduction in blood cholesterol of 24 per cent, 79 per cent were symptomatically benefited. In the control group 65 per cent of the patients showed an average reduction in blood cholesterol of 5 per cent, and 64 per cent showed symptomatic benefit.
- 4 Among the surgical patients who had symptoms after cholecystectomy and were treated with the low cholesterol diet, 10 per cent of those showing a reduction in blood cholesterol were not benefited. In the control group 40 per cent were not benefited.
- 5 Minimum readings of the blood cholesterol were obtained within the first 8 months for 93 per cent of the medical patients on the low cholesterol diet, whereas after cholecystectomy minimum figures were obtained only after 8 months for 50 per cent of the patients.
- 6 Twelve patients with gall-bladder disease and a normal value for blood cholesterol preoperatively had hypercholesteremia after cholecystectomy

The authors concluded that

- 1 The low cholesterol diet has been found by repeated chemical analyses to reduce the blood cholesterol in cases of hypercholesteremia
- 2 The low cholesterol diet gives symptomatic relief in most of these cases.

3. The diet is indicated after cholecystectomy, to preclude hypercholesteremia and recurrent symptoms.

Jaundice

Vitamin K and Obstructive Jaundice—A long series of researches in basic medical sciences has in the past year apparently culminated in the solution of one of the most perplexing of clinical problems; the explanation and methods for the control of the hemorrhagic diathesis of jaundice.

A. C. Ivy and J. S Gray¹⁹ point out that this series of researches began in 1929 when Dam placed chicks on a synthetic diet containing only cod-liver oil as a source of the fat-soluble vitamins in order to conduct experiments on the cholesterol metabolism. It was noted that the chicks developed a syndrome characterized by severe subcutaneous and intramuscular hemorrhages and erosions of the lining of the gizzard Although these symptoms suggested a deficiency of vitamin C, Dam was unable to control them by the administration of lemon funce.

McFarlane, Graham and Richardson observed a similar hemorrhagic condition in chicks reared on an ether extracted diet Blood from these animals was observed to remain uncoagulated when allowed to stand over night Holst and Halbrook made the same observation, but suspected a vitamin C deficiency, since the condition responded to the inclusion of cabbage in the diet. In 1934 Dam and Schonheyder reported that cereals contained adequate amounts of a curative substance. Their finding that ascorbic acid and cod-liver oil failed to influence the hemorrhagic tendency definitely eliminated vitamins A, D, and C. In addition to gross spontaneous hemorrhages the deficient chicks failed to grow normally and exhibited severe anemia. Since the most characteristic symptom appeared to be a loss of blood coagulability (spelled with a K in the Germanic languages), the new vitamin was given the name of vitamin K. Subsequent investigation revealed that the gizzard erosions were due to the absence of an entirely different dietary factor.

Schonheyder has shown that the enormous delay in coagulation time in chicks deficient in vitamin K is not due to a disturbance in the fibringen, calcium, or cellular elements of the blood, or in the thrombokinase content of the tissues. Some constituent of normal blood plasma was absent, however, for the addition of normal plasma to the blood of bleeding chicks restores the coagulation time to normal. The deficient element in the coagulation process was shown by Dam, Schonheyder, and Tage-Hansen to be prothrombin. Although vitamin K itself could not behave in vitro as prothrombin. inconclusive evidence was obtained that vitamin K might be a constituent of prothrombin, perhaps a prosthetic group of the prothrombin complex. By a more convenient and accurate method, which involved the same principles as Quick's method for the determination of prothrombin (vide infra), Schonheyder has demonstrated an almost complete disappearance of prothrombin from the blood of chicks deficient in vitamin K. According to the results of Dam, Glavind, Lewis and Tage-Hansen, the intravenous or intramuscular injection of vitamin K concentrates in the form of an emulsion reduced the coagulation time within an hour The vitamin was ineffective when administered subcutaneously unless it was dissolved in water with the aid of desoxycholic acid

Vitamin K was reported by Dam to be present in high concentration in hog liver and in certain seeds and green leafy vegetables, but to be absent from wheat-

germ oil. The latter finding clearly differentiated it from vitamin E. It was found to be a fat-soluble vitamin, present in the nonsaponifiable but nonsterol fraction of extracts from potent sources. These findings in regard to the chemical behavior of the vitamin were confirmed promptly and independently by Almquist and Stokstad, who continued the investigations of Holst and Halbrook mentioned previously. Almquist later prepared a material which underwent crystallization at low temperatures and which when added to the diet of chicks in quantities of from only 2 to 4 mg. per kg. of food protected chicks against deficiency symptoms. More recently Almquist and Klose have prepared a crystalline derivative of vitamin K by conjugation with cholic acid. The free vitamin is apparently an oily liquid at rcom temperatures. It has not yet been synthetized, nor has its chemical structure been elucidated

The real significance of vitamin K for mammalian physiology and for clinical medicine was revealed by investigations along a different line. An enormous literature relative to the coagulation defect in the hemorrhagic diathesis of jaundice had accumulated. This work merely served to prove quite conclusively that bleeding in jaundice is in no way related to a disturbance in fibrinogen or calcium levels of the blood, to a deficiency in the formed elements of the blood, nor to any other easily studied component of the clotting mechanism

Until a few years ago the only available method for the determination of the prothrombin level of the blood was Howell's prothrombin time. Since this method consisted of determining the clotting time of recalcified plasma, it obviously was not specific for prothrombin. In view of this situation, Quick, Stanley-Brown and Bancroft in 1935 devised a

more specific method for the determination of blood prothrombin, the only well known element of the clotting mechanism which had not been adequately studied In this method the most important variable, the thrombokinase, or platelet or tissue factor, is controlled by adding an excess of this substance to plasma before determining the coagulation time. By this method these authors were able to reveal a prothrombin deficiency in the blood of jaundiced patients exhibiting a hemorrhagic tendency. Warner, Brinkhous and Smith devised a still more accurate and specific method for the determination of the concentration of prothrombin in the blood. This method was applied by Hawkins and Brinkhous to the study of the bleeding tendency which was previously observed to occur in dogs with chronic biliary fistulas. In such animals they observed a marked deficiency in the prothrombin level of the blood, which together with the bleeding could be prevented by returning bile to the intestinal tract

J D Stewart²⁰ reports the results obtained in 13 patients, of whom 12 had obstructive jaundice of varying degrees from liver damage, and were given vitamin K-cholic-acid mixture preoperatively Plasma concentrations of prothrombin and bihrubin were determined. The average increase in plasma prothrombin under vitamin K therapy was 328 per cent. The average duration of treatment was 3\%\cap{10}\) days, with an average dose of 68 Gm. The vitamin K extract was prepared from fresh spinach, according to the method of Dam

The plasma prothrombin concentration in 5 patients suffering from massive post-operative hemorrhage is given. In 3 of these, the vitamin K-cholic-acid mixture was given immediately and the bleeding ceased, with a dramatic rise in plasma prothrombin. One patient developed se-

vere diarrhea when the mixture was given through a jejunostomy and the bleeding was uncontrolled. In another patient, given the vitamin K-cholic-acid mixture through a jejunostomy, there resulted a restoration of the plasma prothrombin and a control of the bleeding tendency.

thrombin concentration immediately after operation. This fall was only transitory if vitamin K-cholic-acid feeding was resumed immediately. It was stated that a safe preoperative plasma prothrombin level should preferably be above 75 per cent. Since these levels change frequently, determinations should be made

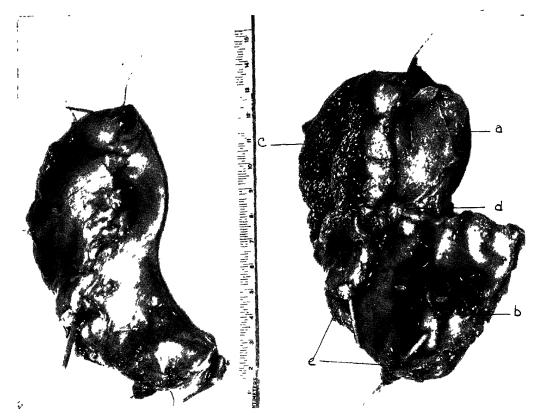


Fig 6—Photograph of the unopened specimen Wooden probes in cystic ducts

Fig 7—Photograph of the open specimen, with lettering corresponding to Figure 8 (a)

Empyema cavity, (b) cavity containing 5 gall-stones, (c) "strawberry" gall-bladder, (d) thick septum of fibrous tissue separating empyema cavity, (a) from cavity containing gall-stones (b), (e) cystic ducts. The pale, smooth lining of cavities (a) and (b) shows the effect of the chronic inflammation, and their thick, edematous walls is evidence of the acute inflammation. (Wilson: Ann. Surg.)

The author noted that in only 1 patient observed, in whom there was obstruction of the bile flow for more than a week, was there an associated plasma concentration level of less than 84 per cent. In this 1 case, the patient's appetite remained good and the biliary obstruction was incomplete. There was a drop of from 20 to 40 per cent in plasma pro-

often and early during the postoperative period. There were 2 patients who refused to take the vitamin K-cholic-acid mixture by mouth because it gave them epigastric distress; after a consequent massive hemorrhage, they co-operated by taking the mixture, with a resulting rapid restoration of plasma prothrombin levels to normal and cessation of bleeding

GALL-BLADDER

Congenital Malformations

While variations from the usual distribution of the biliary ducts are common, duplication of the gall-bladder is relatively rare, occurring about once in every 3000 to 4000 human beings. A satisfactory embryologic explanation of these anom-

(1) Acute cholecystitis; (2) chronic cholecystitis; (3) cholelithiasis; (4) cholesterosis; and (5) empyema. The microscopic examination showed, in addition, a papilloma of the gall-bladder.

Congenital Choledochus Cyst

P. Bull²² states that there are now about 100 known cases of this disorder.

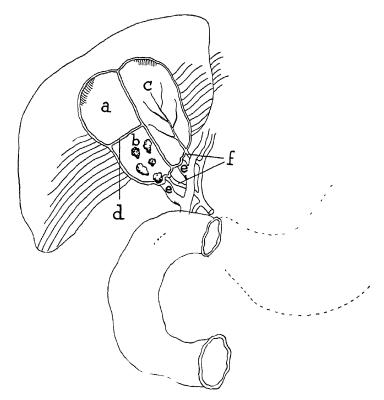


Fig. 8—Diagrammatic drawing of specimen removed. (a) Empyema cavity, (b) acutely inflamed cavity containing gall-stones, corresponding to the pouch of Hartmann, (c) second gall-bladder, separated from the first by a common wall, seat of cholesterosis, (d) septum of chronic inflammatory tissue separating empyema cavity (a) from acutely inflamed cavity containing stones (b), (e) cystic ducts, (f) cystic arteries. (Wilson Ann Surg.)

alies in man is difficult or impossible. C. L. Wilson²¹ has reviewed the literature and has found 36 cases reported up to January, 1936. A case of double gall-bladder with 2 cystic ducts, found at operation, is presented. It is interesting not only because of the anomaly, but because of the several types of gall-bladder disease present in the specimen removed.

The gross pathologic examination shows the 5 stages of gall-bladder disease

Only 5 cases have been recorded in patients over 41. His patient, a woman aged 42, had abdominal pain, probably due to the biliary disturbance, during childhood and a symptom-free period between the ages of 18 and 31 and transient jaundice 2 years later. On gastrojejunostomy for a callous pyloric ulcer when the patient was 35, no tumor was discovered. Seven years later there was pain in the epigastrium radiating to the

spine, with dyspnea; a round, tender, fluctuating tumor, thought to be a retroperitoneal cyst originating from the pan-

creas, filled the epigastrium. After puncture and removal of 2250 cc. of thick dark fluid idiopathic dilatation of the

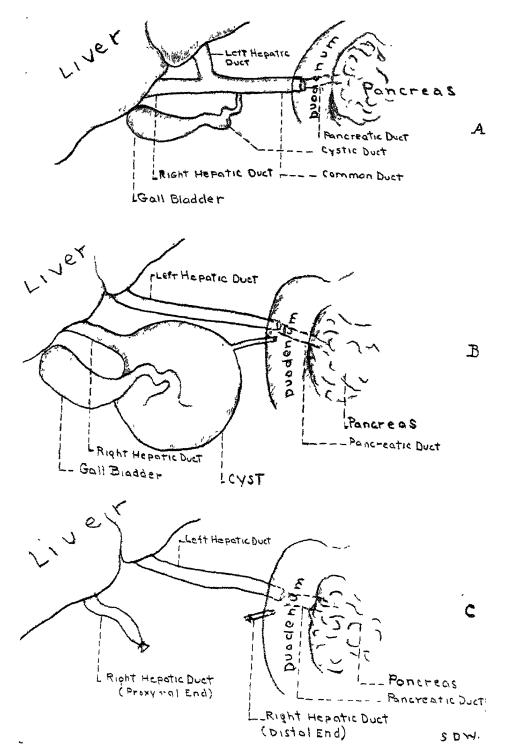


Fig 9—Diagrammatic sketches showing: (A) Normal arrangement of bile passages (B) Present case of double common duct with choledochus cyst before operation (C) Resultant postoperative anatomy (Weeder Ann Surg)

common bile duct was diagnosed. Cholecystoduodenostomy was done. Grave infection in the cyst followed and 3000 cc. of fetid fluid was removed on repuncture; hemorrhagic nephritis and hypochloremic uremia developed. Recurring retention necessitated a third puncture and drainage, with removal of 1500 cc. of fetid pus. Steady improvement set in and on discharge no tumor was palpable.

The author says that idiopathic dilatation of the common bile duct predominates in women. The cardinal symptoms are pain, tumor, and jaundice. Grave complications may occur; the contents of the cyst may become infected before or after anastomosis between the cyst and the intestine, there may be a marked hemorrhagic diathesis, and in rare cases the cyst may rupture into the abdomen Correct diagnosis before operation is said to have been made in only 5 or 6 cases The prognosis depends first of all on the patient's condition at the start of surgical treatment The mortality of the known cases is about 60 per cent. All authors agree that a communication must be established between the bile duct and stomach or intestine, whether primarily or after preliminary drainage; secondary anastomosis must not be long delayed.

A choledochus cyst with a double common bile duct is reported by S D Weeder^{2,3} in a male child operated upon in 1932 The choledochus cyst was excised, after finding what was thought to be a patulous duct running from the porta hepatis to the duodenum. It seemed that the right and left hepatic ducts were separate, and did not join, as is normal, but proceeded separately to the duodenum; and that the choledocus cyst and gall-bladder were a part of the right hepatic duct, the distal end emptying into the duodenum which was not patulous This duct was ligated on both sides of the cyst.

The author prognosticated then that: (1) If the duct to the choledochus cvst was the right hepatic and it was ligated. atrophy of the right half of the liver must follow; bearing out the principle when the need for function ceases, function will cease and the part will undergo atrophy of disuse. (2) If atrophy of the right half of the liver occurs, then there should be a compensatory hypertrophy of the left half of the liver. (3) Compensatory hypertrophy of the left half of the liver will only occur if the left hepatic duct is sufficiently large to adequately take care of the increased secretion of bile. All of these conditions The patency and adecame to pass quate size of the duct were demonstrated by the fact that, since a month after operation until the time when Weeder reported this case, there had never been any suggestion of jaundice. Atrophy of the right half of the liver and compensatory hypertrophy of the left half were demonstrated at the time of a subsequent operation, in 1936, when the abdomen was again opened

The opportunity was offered at that time for Weeder to verify his previous prognostications The right lobe of the liver was atrophied, the left lobe greatly There was a moderate hypertrophied amount of cirrhosis of the liver. bile duct was visualized in the gastrohepatic omentum passing from the porta hepatis to the duodenum There was some increase of peritoneal fluid veins of the peritoneum and the omentum were greatly enlarged. The spleen filled the left half of the abdomen. was removed without difficulty, and a blood transfusion of 150 cc. given.

Acute Cholecystitis

A review of the case histories of 219 patients with acute cholecystitis who

have been treated at the New York Hospital in the past 6 years is given by F. Glenn.²⁴

The diagnosis, "acute cholecystitis," in this group of cases is based upon both clinical and pathological findings Clinically, it has been reached by careful shoulder or back. Nausea and vomiting frequently accompany the onset of pain in these cases.

The physical examination reveals marked tenderness and sometimes muscular rigidity in the right upper quadrant. The gall-bladder may be palpable



Fig 10—Cholecystectomy for acute cholecystitis. The acutely inflamed gall-bladder is readily enucleated from its bed by careful dissection, thus preventing injury to the liver. Although this illustrates cholecystectomy being done by first dividing the cystic vessels and cystic duct, the procedure of first dissecting the gall-bladder from above downward and then dividing these structures is employed by us even more frequently (Glenn Surg, Gynec and Obst)

evaluation of the patient's history, of his symptoms and of the signs elicited on physical examination. In the typical case a fairly long history of recurring episodes of biliary colic frequently precedes the onset of the acute attack, in some, however, there is no record of previous symptoms referable to the gall-bladder. The pain is severe, located in the right upper quadrant, and may radiate to the

as a distended and tender mass. The patient looks ill, has a rapid pulse, some fever, and an elevated leukocyte count. Some patients whose attacks had lasted more than 24 hours showed a nuld degree of jaundice.

Many of the 219 patients failed to present these characteristic manifestations of acute inflammatory disease. In some there was no fever; in others the

leukocyte count was normal, and in still others the symptoms were not acute and, therefore, gave little hint of the seriousness and extent of the inflammatory process. In these atypical cases the final differential diagnosis was made on the basis of the findings at operation and in the pathologist's report.

Free perforation with general peritonitis also may occur. The favorite location for such perforation is shown in Figure 11. This avascular area in the presence of inflammation of the gall-bladder and compression of its blood vessels is most likely to become gangrenous first. Necrosis of this portion of the gall-bladder



Fig. 11—The distended, acutely inflamed gall-bladder. Dotted line indicates area where free perforation is most likely to occur. (Glenn. Surg., Gynec. and Obst.)

At the operating table the surgeon finds a reddened, distended gall-bladder with thick, edematous walls (see Fig 10). Besides one or more stones, the organ usually contains colorless bile or pus under pressure. On close inspection, areas of necrosis and gangrene of the wall may be noted, and in some a frank perforation will be found with inflammatory reaction around the gall-bladder and adhesions to neighboring structures.

in the presence of an increased intracystic pressure results in perforation and escape of the contents of the organ into the abdominal cavity. On gross pathological examination an acutely inflamed viscus with congested walls and areas of necrosis is described; microscopically, the specimen shows polymorphonuclear infiltration with desquamation of the epithelium and necrosis of one or all layers of the gall-bladder.

TABLE 3-ACUTE CHOLECYSTITIS

Extent of Inflammatory Process	Cases	Age	Duration of Disease	Mortality
Total acute cholecystitis	219	Average age 46 years	Average duration 2.7 years	3.19
Acute without gangrene	160	110 less than 50 years 50 more than 50 years	70 less than 1 year 90 more than 1 year	2 5 1 8 8.0 0.0 4.4
Acute with gangrene	41	27 less than 50 years 14 more than 50 years	14 less than 1 year 27 more than 1 year	2.43 3.7 0.0 0 0 3.85
Acute with gangrene and perforation .	18	7 less than 50 years 11 more than 50 years	9 less than 1 year 9 more than 1 year	11 11 0 0 19.9 0 0 22 2

(Glenn: Surg, Gynec & Obst)

Operative Procedure—The operation of choice in acute cholecystitis is a cholecystectomy, for it interrupts the pathological process and prevents the development of its serious consequences. This operative procedure is contraindicated (1) in the presence of peritonitis following perforation of the gall-bladder, (2) in conditions which make it difficult to identify the important structures in the biliary fossa When the gall-bladder is greatly distended and adherent, the adjacent viscera may be so distorted that anatomical relations are obscured, and there would be danger of inadvertently injuring the hepatic vessels or the common duct. (3) It is contraindicated in the presence of severe jaundice caused by obstruction of the common duct. (4) It is contraindicated in patients whose general condition is so grave that a general anesthetic and prolonged operative procedure are not justified In such cases a compromise must be sought in the form of surgical treatment which will tide the patient over the immediate crisis without adding to his burden.

On the basis of the principles enumerated, 200 of the 219 cases of acute cholecystitis were subjected to cholecystectomy and in 22 of these the common duct was explored. In 19 cases cholecystostomy was done. An exploration of the common duct rarely is necessary in acute cholecystitis. Especially is this true of the younger patients, for common duct stones are not often seen unless the disease has persisted for a considerable time. The indications for exploration in acute and chronic disease of the biliary tract are not identical. If there is marked jaundice or a history of recurring attacks of jaundice, and if a stone is palpated in the duct, then the common duct must be explored. The duct may be indurated and may appear to be distended without harboring a stone. An icteric index of 30 or less may be due to an inflammatory process in the biliary tree rather than to obstruction of the duct by a stone. In general it may be said that the common duct should not be explored in acute cholecystitis unless definitely indicated In this series of

cases it was explored 22 times and stones were found and removed in 9.

Analysis of Study—In Glenn's experience the diagnosis of an acute process in the gall-bladder is not difficult. However, the differential diagnosis of simple acute and complicated acute

When the gall-bladder is acutely inflamed, it is easily stripped from its bed without injuring the liver and other neighboring structures (see Fig. 10). The difficulties of the operation for acute cholecystitis are encountered in cases which have been permitted to proceed to

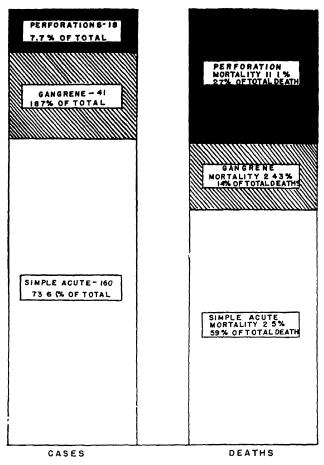


Fig. 12—Chart showing in left column comparative incidence of 3 types of acute cholecystitis (219 cases), right column, comparative mortality in 3 types of cases of acute cholecystitis (7 cases) (Glenn - Surg., Gynec & Obst.)

cholecystitis is very difficult, for the complications such as gangrene and perforation may occur in the presence of subsiding symptoms and normal temperature and leukocyte count. Only by planning an early surgical attack in acute cholecystitis can we hope to lower the mortality. Delay in operating tends only to increase the hazard of gangrene and perforation

gangrene and perforation or in those cases in which the disease has subsided, leaving the patient with an extracholecystic abscess or adhesions.

It is repeatedly stated in the literature that the removal of an acutely inflamed gall-bladder is likely to be attended by the extension of the infection. This danger, in Glenn's opinion, is greater when an extracholecystic abscess or a localized

peritonitis exists. It is true that streptococcic infection of the biliary tract is not uncommon; also, that these infections tend to spread when disturbed by operation. When great care is used not to spread the infection during operation, it has been demonstrated that fulminating streptococcic infections after cholecystectomy do not occur Furthermore, contamination of the operative field with the contents of an acute inflamed gall-bladder does not invariably lead to extensive peritonitis. Drainage is applied in all cases at operation.

The postoperative course in patients under 50 years of age with simple acute cholecystitis is almost invariably uneventful. The older patients obviously are more likely to suffer postoperative complications. However, if time is taken before operation to counteract conditions such as dehydration, cardiac decompensation, etc., and the operation is planned so that it places little additional burden on the patient, the incidence of postoperative complications will be no higher during the acute stage of cholecystitis than in chronic affections of the gallbladder It would seem that the danger of operating in uncomplicated acute cholecystitis is overemphasized. It is, Glenn believes, distinctly less than the danger of gangrene and perforation which occur in a fair percentage of cases if a waiting policy is pursued

The mortality rate was 3 19 per cent for the 219 cases irrespective of pathology, age, or other factors. Compared to the mortality rate for all operations for nonmalignant disease of the biliary tract, which includes a series of 905 cases, this is a favorable figure. It must be stated here that the operations were performed not by 1, but by 12 or more general surgeons.

It is shown by this series of cases that early operation may not be difficult nor attended by a greater incidence of complications nor a higher mortality rate than that ordinarily reported for series of operations for diseases of the gallbladder.

It is further shown that the outcome of an inflammatory process in the gall-bladder is unpredictable. Therefore, delay in operating may lead to serious complications which greatly increase the difficulty of operation and the attendant mortality.

It is shown that the younger the patient when subjected to operation, the better the chance of an uneventful recovery and good end-result.

On the basis of these findings it is recommended that disease of the biliary tract be treated surgically as soon as the diagnosis is made unless the general condition of the patient makes such treatment dangerous without preoperative therapy.

If this policy is pursued, the author believes that the mortality rate in surgery of acute cholecystitis will be diminished and, perhaps, the progress of certain systemic diseases, such as cardiovascular and hypertensive disease, may be retarded.

Noncalculous Cholecystitis

The results following removal or drainage of the gall-bladder that is free from stones are so unsatisfactory that serious effort should be made to discriminate more closely as to when operation should be advised. There are many patients suffering from noncalculous disease who are relieved by cholecystectomy. They must be differentiated from those whose symptoms, while similar, have their origin in the colon, spine, duodenum, or other adjacent organs.

According to W. H. Cole,²⁵ the types of noncalculous lesions of the gall-bladder

capable of producing symptoms can be divided into 6 groups:

- Acute inflammation About 10 per cent of the patients with acute cholecystitis have no stones in their gall-bladders. The actual mechanics of the production of the acute inflammation are no doubt different in calculous and noncalculous cholecystitis, but the pathological and clinical results may be quite identical. In approximately 50 per cent of the cases of acute inflammation, positive cultures are found on bacteriological examination Nonbacterial inflammation therefore accounts for a large percentage of cases Andrews has noted that acute cholecystitis can be produced experimentally by injecting bile into the gall-bladder "in concentrations only 1 or 2 per cent more than the 6 or 8 that are found in normal human bile." Patients with noncalculous acute cholecystitis appear sicker, more frequently have chills, and maintain a higher temperature range than those with acute cholecystitis caused by stones in the cystic duct
- 2 Chronic inflammation. In the majority of instances chronic noncalculous cholecystitis, as characterized primarily by thickening of the gall-bladder wall and lymphacytic infiltration, does not arise as a sequel of acute inflammation but develops insidiously. In either the chemical or bacterial chronic cholecystitis, the wall may be so hadly damaged as to destroy practically entirely the function of the gall-bladder It has been shown by numerous observers that the secretory pressure of the pancreas is greater than that of the liver. In the human being any obstruction at the sphincter of Oddi distal to the junction of the choledochus and the duct of Wilsung, regardless of whether it is produced by stone or spasm, might allow the entrance of pancicatic secretion into the common duct and gall-bladder with the subsequent production of cholecystitis. The actual importance of noncalculous cholecystitis lies in the observation that, in general, cholesterol stones are produced by short periods of obstruction at the cystic duct and calcium stones are produced by long periods of obstruction. primary factor under these circumstances would have to be noncalculous in origin
- 3 Lesions of the cystic duct. Obstruction to the cystic duct may be unmistakable and may even be so severe as to produce a complete obstruction. The 3 patients described by the author appears to illustrate 3 of the important types of obstruction: Angulation of

- the duct; stenosis, and anomalous excessive Heisterian folds. While no positive proof can be offered that lesions of the cystic duct as described in these 3 patients were the primary cause of the patients' complaints, nevertheless, the wall of each gall-bladder was so slightly diseased and the common duct appeared so normal that the author believes himself justified in suspecting the cystic duct of being the major factor in the production of the symptoms.
- 4 Biliary dyskinesia. Under normal circumstances the secretory pressure of bile in the liver, which varies between 300 and 360 mm. of water is far higher than the pressure of 100 mm of water necessary to break through the sphincter of Oddi Occasional instances have been reported in which sufficient spasm of the sphincter of Oddi has been noted postoperative to produce symptoms and to require a pressure of 160 mm. of water to break through it In such instances the pain complained of is similar or identical to that noted before operation Nitroglycerin (glyceryl trinitrate) relieves the pain produced by this spasm. The rise in pressure within the common duct from 0 to from 200 to 350 mm of water, as produced by the hypodermic injection of morphine, may at times be associated with pain in the upper abdomen. This pain and discomfort are not unlike that experienced by many patients with supposed gall-bladder dis-Although it appears that the paralysis ease of the sphincter of Oddi as noted after cholecystectomy is usually permanent, instances have been reported in which a spasm of the sphincter of Oddi was noted postoperatively It is apparent that this spasm may be responsible for the patient's symptoms and failure to obtain relief. It is barely possible that in many instances relief of symptoms following operation is dependent upon a paralysis of the sphincter of Oddi. It appears that this group of patients who have persistent symptoms following cholecystectomy and in whom spasm of the sphincter is demonstrable may be classified as belonging to the group of patients with biliary dyskinesia
- 5 Metabolic disturbances in the biliary system. It seems likely that most of the pathological metabolic findings are of importance chiefly in relation to the ultimate production of stones or to the depositions of calcium in the wall of the gall-bladder. The change in the bile-salt-cholesterol ratio in the etiology of cholesterol stones has been emphasized.

6. Cholesterosis. There is a growing disbelief in the relationship between cholesterosis and symptoms of gall-bladder disease. Gallstones will be found to accompany cholesterosis in from one-third to one-half of the occasions on which it is noted at the operating table. It is particularly noteworthy that excision of the gall-bladder in the presence of cholesterosis without stones is followed by poor results. It is therefore doubtful if cholesterosis has anything to do with the production of manifestations attributable to disease of the gall-bladder.

It appears logical to assume that no single factor is responsible for cholecystitis. Many factors, including acute and chronic infection of the gall-bladder, chemical inflammation, obstruction of the cystic duct, biliary dyskinesia, and perhaps others, are important in the pathogenesis of gall-bladder disease.

Further evidence that pancreatic reflux is an etiological factor in gall-bladder disease is presented by J. A. Wolfer.²⁶ It has been suggested that obstruction of the cystic duct represents the primary cause of gall-bladder disease and that infection, when it does occur, is a secondary phenomenon. In many instances, however, no obstruction can be found Judd suggested a possible chemical cause for disease of the gall-bladder in these cases. Wolfer, as a result of considerable experimentation on dogs, has been able to show that pancreatic juice, when introduced into the gall-bladder, produces pathological changes in the wall of the gall-bladder, and the possibility that pancreatic juice may enter the gall-bladder has been demonstrated. India ink introduced into the terminal end of the common duct of the dog was later recovered in the gall-bladder Attention was also called to the anatomically proved common pathway between the pancreatic and biliary tracts in 284 of 652 specimens examined by various investigators Also, recent cholangiographic studies have

demonstrated a physiological common pathway between the 2 ducts.

Any obstruction at the sphincter of Oddi, be it spastic or organic, will result eventually in the passage of pancreatic juice into the gall-bladder in those instances in which a common pathway is present. The agent which activates the pancreatic juice may be enterokınase (supposedly derived from the mucosa of the gall-bladder), a substance liberated by broken-down cells, or contaminated pancreatic juice. One-tenth normal sodium bicarbonate solution (the concentration of alkalinity in pancreatic juice) may also produce a violent reaction in the mucous membrane. With the theory that the reflux of the pancreatic juice may be the cause of gall-bladder disease in mind, it is recommended that some widespread observations be carried out. They should include the following: (1) Repeated examinations of the drainage for amylase in all cases of gall-bladder and common-duct drainage; (2) cholangiographic studies to visualize the pancreatic duct in all cases of gall-bladder and common-duct drainage; and (3) study of the possibility of early history which is suggestive of biliary dyskinesia in all cases of gall-bladder and duct disease

Additional evidence of regurgitation of pancreatic juice into the gall-bladder is furnished by H Mehnen ²⁷ He describes 4 different types of the opening of the common bile duct and the pancreatic duct into the intestine. He had investigated 449 cases and found a separate opening into an individual papilla in 19, a separate opening into a common papilla in 151 cases and a common opening with formation of a diverticulum in 248 cases, while in 27 cases the pancreatic duct and the choledochus entered the duodenum about 8 mm. away from the papilla of Vater without formation of a diverticulum Thus the anatomic relationships found

made it possible in 61.25 per cent of the cases for regurgitation of pancreatic juice into the gall-bladder in the cases of obstruction in the opening of the ducts into the intestine

The author had established that among the 275 cases presenting the possibility of regurgitation of pancreatic secretion there were 35.3 per cent instances of gall-stones, while in 174 cases with separate openings the stones were found in only 14.4 per cent. The incidence of cholesterol-pigment-calcium stones in joint opening of the ducts as opposed to that of cases in which there was no possibility for back flow was as 4.1 and the incidence for pure cholesterol stones as 7:1, while for pure pigment stones it was as 1.5. The author investigated 200 cases with regard to the gall-bladder content. The characteristic sediment in cases of joint opening of the large ducts consisted of cholesterol crystals, while that for the separate openings were bilirubin concrement The author interpreted these observations by assuming that the regurgitation of the pancreatic juice into the gall-bladder leads to dimmution of biliary acids and therefore to precipitation of cholesterol, which in turn favors the formation of cholesterol-pigment-calcium stones and particularly the formation of pure cholesterol stones. The fact that of the 29 cases of strawberry gall-bladder 25 presented the possibility of regurgitation of pancreatic ruice supports the concept of the disturbance of the solubility of cholesterol through the regurgitation of pancreatic secretion.

Carcinoma of the Gall-Bladder

The incidence of carcinoma of the gallbladder appears to vary considerably, and depends largely upon the source from which the statistics are drawn. Next to the immediate operative mortality following cholecystectomy for cholecystitis, the

TABLE 4—INCIDENCE OF CARCINOMA OF THE GALL-BLADDER IN CHOLELITHIASIS

Author	No of	No. of Cases	Incidence of
	Cases of	Associated With	Carcinoma
	Cholelithiasis	Carcinoma	(Per cent)
Lentze Heyd Deaver and Bortz Schroeder Graham Fawcett and Rippmann Riedel Slade Candler Judd and Gray Illinois Research Hospital, Chicago	557	25	4 3
	330	13	4 0
	450	13	2 9
	141	20	13.4
	564	48	8 5
	592	48	8.1
	300	13	4.3
	17	10	59.0
	315	2	0.6
	15,422	312	2.0

(Cole Surg, Gynec & Obst)

death rate incident to carcinoma of the gall-bladder is probably of more significance from the standpoint of life insurance than any other disease affecting the gall-bladder. W. H. Cole²⁸ points out that carcinoma of the gall-bladder is an extremely malignant tumor, the 5-year survival rate including the operative as well as the nonoperative cases being considerably less than 10 per cent. The most important features of carcinoma of the gall-bladder, particularly in regard to life insurance, are related, therefore, to its incidence

After a rather extensive study, Rolleston and McNee found that the incidence of carcinoma of the gall-bladder in chole-lithiasis varied between 4 and 15 per cent. The figures given in Table 4 represent those found in 11 consecutive reports encountered in a survey of the incidence of carcinoma of the gall-bladder. The variation of incidence from 0 6 to 13 4 per cent is so extreme that it would appear hopeless and inaccurate to attempt to arrive at an average figure from this group of reports. When a percentage is given, specifications should be

made as to the source of the cases studied, i. e., whether they were taken from autopsy or operative records, because the incidence should be lower in a group of patients who are operated upon than in a group of autopsy cases since the patients in the latter group will be older. The low incidence of 2 per cent reported by Judd and Gray may in part be explained on this basis, since their figures are taken from operative cases. This is even lower than that of other reports dealing only with operative figures. There may be an additional factor of considerable importance, namely, the fact that jaundice and weakness develop insidiously without much pain in carcinoma of the gall-bladder and when the patients are seen by physicians they appear too ill to travel as far as the Rochester Clinic, which derives its patients largely from out of town scarcely appears possible to assume that the hereditary characteristics of cancer are strong enough to explain a high incidence of carcinoma of an organ in one locality and a low incidence in another, although there can be no doubt regarding the existence of "cancer families" Judd and Gray reported that of 312 cases of carcinoma of the gall-bladder and bile ducts, 32 per cent occurred in the ducts.

The relationship of gall-stones to the development of carcinoma of the gall-bladder has long been known. The incidence of stones in carcinoma of the gall-bladder varies between 69 (Stewart) and 100 per cent (Mentzer). An average of 8 large series revealed an incidence of 85 per cent.

Considering the data presented, it is obvious that the incidence of carcinoma of the gall-bladder in cholelithiasis is significant, and that the high incidence (85 per cent) of stones in carcinoma of the gall-bladder is an important factor in its etiology. Graham and others have called

attention to the fact that cholecystectomy in the presence of cholelithiasis undoubtedly saves the lives of many people who otherwise would die from carcinoma of the gall-bladder. It is true, however, as noted in Table 4, that the relationship of carcinoma of the gall-bladder to cholelithiasis is extremely variable. Undoubtedly the percentage would be much smaller if the survey were to include cases of cholelithiasis not confined to the hospital. Patients coming to operation for cholelithiasis would doubtlessly be older than the patients with cholelithiasis not confined to a hospital persons with cholelithiasis coming to autopsy would be still older In other words, the danger of development of carcinoma of the gall-bladder would in a general way increase with age and the length of time during which the individual has had the stones.

Investigations as to the typical features of cancer of the *lower end* of the *common duct* are becoming of increasing importance, and in recent years attempts at surgical removal of the cancer have been made with considerable success. The report of J. C. Dick,²⁹ comprising 13 cases, gives the main characteristics of carcinoma in this situation, and at the same time shows how hopeful the field is for the surgeon

An analysis of 4239 consecutive autopsies performed in the Glasgow Royal Infirmary shows that cancer of the gall-bladder had occurred 20 times, cancer of the biliary tract 18 times, and cancer of the ampulla of Vater, 6 times Altogether, these cases represented by 1 per cent of all the autopsies, yet the 18 cases of carcinoma of the bile ducts in 4239 autopsies (0.42 per cent) showed that cancer in these passages is not so rare as is generally believed. Interesting facts were shown by an analysis of the numbers of cases with gall-stones, 18 of 20 cancers

of the gall-bladder presented calculi, whereas only 2 of the 18 cancers of the bile ducts were associated with stones in the gall-bladder or bile ducts. The sex incidence also differed greatly in carcinomas of these situations. There were more than twice as many cases of cancer of the gall-bladder in women as in men, whereas bile-duct cancer occurred only slightly more often in men than in women In the majority of patients, the condition made its appearance between the ages of 50 and 69 years

The majority of the author's cases of cancer of the lower end of the common bile duct presented a similar macroscopical picture. The tumor was situated within the lower 2 cm of the duct Above the growth there was marked dilatation and sacculation, with deep bile staining of the wall of the duct. The dilatation extended back into the hepatic ducts and the small bile ducts within the liver. In a few instances, suppurative cholangitis was superadded. The cystic duct and the gall-bladder were also dilated. At the lower end of the common bile duct, the tumor caused stenosis amounting to almost complete obstruction The tumor was usually very small in extent and might easily have been mistaken for cicatricial contraction after ulceration, following the passage of a gall-stone. Local extension and secondary growths in this type of cancer were unusual—a fact that has attracted the attention of others and has proved to be one of the chief indications for the attempt at surgical removal when this condition is suspected Histologically, most of these tumors were adenocarcinomas.

Mortality in Gall-bladder Disease

W H. Cole³⁰ states that the mortality following operations for gall-bladder disease in various clinics is extremely variable, partially because of coincidence

alone, but especially because of the type of patients from which the figures are drawn. In other words, did the patients have uncomplicated cholecystectomies or did complicating lesions, such as suppurative cholangitis and inoperable carcinoma of the gall-bladder, accompany the gall-bladder disease? The analysis of a series reported by Heyd illustrates this point decisively, insofar as the mortality of 557 operations on the biliary tract (with various complications) was 7.0 per cent, but only 3.3 per cent in 500 noncomplicated cholecystectomies. Heyd noted further that the mortality of all types of gall-bladder disease in 417 private cases was only 48 per cent, but in 140 charity patients it was 13.5 per cent. The mortality in choledochostomy for stones in the common duct will naturally be higher than the mortality of uncomplicated cholecystectomy, as is illustrated by the figure of 87 per cent reported by Eliason and Erb and 12 per cent by Mathews. After reviewing the results of various surgeons, Cole estimates the mortality in common-duct surgery throughout the United States not to be much lower than 10 per cent. As stated previously in a survey of numerous reports in the literature. Hener found a mortality of 8 per cent in 1066 cases of acute cholecystitis, while in 502 cases of gangrene with perforation of the gallbladder there was a mortality of 46 per cent. In his survey of 36,623 operations for gall-bladder and biliary-duct disease, he found an average mortality of 6.6 per cent. This probably represents a fairly accurate estimation of mortality when all types of patients and operations are considered

From the above data it can readily be discerned that the mortality following gall-bladder operations varies considerably and depends upon numerous factors, one of the most important of which is the

operability of the patient. Cholecystectomy for gall-bladder disease in the absence of complications, in the author's experience, is not associated with a mortality greater than 1 or 2 per cent. On the other hand, in elderly patients with myocardial or renal damage, the expected mortality may be as high as 25 per cent. The age of the patient is no doubt an important factor in mortality. For example, Goldish and Gillespie noted that in a series studied by them the average age of patients dying following gallbladder operations was $10\frac{3}{10}$ years more than the average age of the patients who survived the operation Obviously, cholecystectomy should not be performed promiscuously on patients who are poor risks, but not infrequently symptoms are so severe as to demand an operative procedure of some type. In this group of patients cholecystostomy will be much safer than cholecystectomy and may afford relief for the few years of life remaining. Although the mortality following cholecystostomy, as practiced during recent years (14 per cent in a recent series reported by Heyd), is even higher than that following cholecystectomy, the explanation can readily be found in the fact that cholecystostomy now is being performed only on the patients who are seriously ill Even simple procedures will be associated with a high mortality.

Obviously, if extreme care is exercised in estimating the operability, choosing the right time for operation, treating patients preoperatively, and performing the type of operation most suitable for the patient, the mortality will be lowered. For example, over a 3-year period Graham was able to reduce his mortality in cholecystectomies from 60 per cent to 04 per cent by utilizing the precautions mentioned above and paying particular attention to the liver-function test as a means of computation of operability.

For some unexplainable reason, women tolerate gall-bladder operations much better than men. Almost invariably, in a large series, the operative mortality will be from 2 to 3 per cent higher in men than women. The mortality is usually higher in negroes than in white people. In a series studied by Boyce and associates, it was found that the incidence of gall-bladder disease in negroes was only one-fifth as great as that in white patients, but the mortality was higher, being 136 per cent; this was approximately 5 per cent higher than the mortality in the white patients of their series.

As intimated previously in this report, the question has been raised by many authorities as to whether the life expectancy in a patient whose gall-bladder has been removed is not shortened This question has been answered at least to some extent by Dublin and associates in their analysis of a group of people insured in the Metropolitan Life Insurance Company In the group who had drainage of the gall-bladder (cholecystostomy) the actual death rate was 155.7 per cent of the expected rate. The group which had drainage of the gall-bladder for stones had a still higher death rate, namely, 2149 per cent. In the group which was treated medically the death rate was 115.1 per cent of that expected The lowest death rate, 959 per cent of the expected rate, occurred in the group of patients who had had the gall-bladder removed Although the life span in this group of people having had cholecystectomy was greater than that for the average individual, the difference was so slight that factors, such as coincidence, might explain the observation In consideration of all the groups stud-1ed, the death rate was higher among the men than among the women. An analysis of the cause of death in the group in

which the death rate was excessive, revealed the remarkable fact that death was due, for the most part, to malignant or nonmalignant diseases of the digestive tract. This is difficult to explain unless erroneous diagnosis and complications of gall-bladder disease could be considered factors.

An analysis of the causes of death reveals the fact that the factors responsible for death are innumerable, but more important is the lamentable fact that peritonitis is the most frequent cause of death. Probably the most extensive study made is that reported by Stanton who analyzed 500 deaths following gall-bladder operations. The percentage of deaths caused by peritonitis approaches quite closely that reported by Colp and Ginsburg. In each series the percentage of deaths attributed to pneumonia is approximately 10 per cent.

In a much smaller series, Heyd noted that approximately 20 per cent of the deaths were attributed to hepatic insufficiency. Although only 38 per cent of the cases studied by Stanton resulted in death due to hepatic insufficiency, it would appear that the major factor in many other groups, such as "cholemia," "cholemia with hemorrhage," "high temperature," "renal failure," and perhaps others, may be attributable to hepatic insufficiency

Contrary to what might be expected, the incidence of evisceration as a cause of death was surprisingly low, being 0.2 per cent in one series and 3.1 per cent in the other. Maes and his associates have called attention to the fact that the high incidence of death in patients who have suffered evisceration is not attributable directly to the evisceration itself. In other words, post-mortem and clinical studies show quite clearly that death would have occurred anyway in the great majority of cases.

Cholecystectomy

A more or less routine procedure for cholecystectomy by downward dissection is advocated by T. L. Hawkins.31 He states that this procedure may be slower and, if the cystic artery is not previously clamped, more bloody; but he feels that these objections are negligible if such a procedure will lessen the number of inadvertent injuries to the common and hepatic ducts. After the abdomen is opened and the gall-bladder is brought into the field, the liver may be manually rotated or the falciform ligament clamped and used as a retractor to tip the undersurface of the liver to a more unobstructed view. The fundus of the gallbladder is grasped with rubber-covered forceps and traction is applied upward An elliptical incision is made about the grasping forceps through the peritoneal covering of the gall-bladder. With small forceps the peritoneum is grasped and held by an assistant. The initial incision is continued down the inferior surface of the gall-bladder and on to the cystic duct Blunt dissection with small forceps is continued to free the gall-bladder from the liver, and any troublesome bleeding points are cut and clamped. Gauze dissection is not used at any time. As the dissection proceeds downward, another rubber-covered forceps may grasp the gall-bladder lower to bring the cystic duct more directly in the operative field The cystic artery should be ligated separately and for as long as possible so that its ligated end may be finally closed over with peritoneum.

When the junction of the cystic duct with the common duct is clear and distinct the cystic duct is doubly clamped, severed with a cautery and doubly ligated with chronic ligature. Stones may be palpated or the common duct explored at this time, a complete change of abdominal moist packs being inserted as a

quarantine. If there is no jaundice present, the common duct is of normal size, no stones are palpable and aspiration reveals clear light colored bile, further exploration is not necessary. The peritoneal flap resected from the gall-bladder and cystic duct is sutured continuously over the stump of the duct and the ligated cystic artery along the bed of the liver, so that complete peritonealization of the gall-bladder area is obtained. The abdomen in the absence of commonduct drainage is closed without drainage, the only exception being when the gall-bladder has been torn inadvertently.

In draining the common duct there are several pitfalls to be avoided; the incision in the duct need not be larger than to permit the insertion of a folded T drain or the removal of stones. Meticulous attention should be given to the condition of the rubber T tube. It should be thoroughly tested and inspected before insertion to ascertain that the rubber is vital and that no leaks are present.

Morbidity Following Cholecystectomy—A study of the end results obtained in 264 patients (available from a series of 504) who had undergone cholecystectomy is outlined by E. L. Eliason and J. P. North ³² It was found that cholecystectomy gave relief in 94 per cent of the patients whose cases were followed up. The failures were discussed in 4 groups

In the first group there were 8 patients in whom an incorrect diagnosis of gall-bladder disease had been made preoperatively Although these cases had been studied very carefully, cholecystectomy was believed to be indicated. None of the patients was benefited because the principal lesion was outside of the gall-bladder, although several were found to have calculi and pericholecystic adhesions. One of the patients in this group, after 2 years, developed a huge carci-

noma of the greater curvature of the stomach; another had pylorospasms; a third patient had acute serositis of the hepatic capsule and adjoining peritoneum with filmy adhesions, as the result of a gonococcal infection originating in the pelvis. A brief abstract of the 8 failures is presented

Eight patients were placed in a group classified as having had incomplete diagnosis. These patients had definite cholecystic disease which was verified at operation, but, in addition, other pathology was found to be responsible for their symptoms None of the unsatisfactory results in this group was due to undiscovered stones in the duct, despite the fact that only 18 per cent of the total number of operations for inflammatory disease included exploration of the common duct The failures in this group were due to the fact that the patient's suggestive symptoms were thought attributable to the gall-bladder, when in reality the gall-stones were silent and not the chief source of the discomfort.

Fifteen per cent of the cholecystectomies were performed for chronic, non-calculous cholecystitis.

There was a third group of 5 patients who were not relieved of their symptoms until from 6 to 16 months after cholecystectomy had been performed. The authors concluded that probably relief was not obtained in these cases until the ducts had had an opportunity to dilate and, perhaps, assume the function of the absent gall-bladder.

There was a fourth group of so-called extraneous complications which were not biliary in origin and which gave residual difficulty after operation. These were listed as right-sided ureteral colic; ulcerative colitis with epigastric pain; pulmonary and intestinal tuberculosis with dyspepsia; tabes dorsalis with epigastric pain; subacromial bursitis of the right

shoulder; hyperthyroidism; and myocardial disease with fibrillation. The latter 2 were present both before and after gall-bladder operation

This follow-up study did not include any of the patients who had had cholecystostomy.

The late results of the cholecystectomy in a follow-up study of 400 patients operated on at the Medical Institute of Odessa, according to A. G. Sosnovskiy³³ revealed a complete clinical recovery in 82 per cent, improvement in 12 per cent and failure to improve in 5.5 per cent. Recurrent manifestations were present in 4.2 per cent after operations for uncomplicated cholecystitis, in 18 per cent after operations for cholecystitis with complications of medium severity and in 34 per cent after operations for cholecystitis associated with severe complications Recurrence of pain was present in 255 per cent of all cases. In 8 per cent there was pain which lasted for from $1\frac{1}{2}$ to 5 months and was followed by a complete clinical recovery, in 12 per cent the pain recurred for a period of from $\frac{1}{2}$ to 3 years and was followed by considerable improvement, while in 5.5 per cent pain was present for from 3 to 11 years and there was no improvement in the clinical condition of the patient. The author concludes that an early and timely operation when the inflammatory process is localized in the gall-bladder and does not involve the adjacent viscera is essential to the obtaining of satisfactory late results

Cholecystectomy is the operation of choice in cholecystitis. It results in a small mortality rate and is rarely followed by a recurrence. Choledochotomy with drainage of the hepatic or the common-bile duct is indicated in obstruction of the bile passages complicated by cholangitis, hepatitis or pancreatitis. Drainage of the duct may be omitted on the

removal of the obstruction, in the absence of complications and with a patent papilla of Vater. Cholangitis, hepatitis and pancreatitis were the more frequent causes of recurrence. In the majority of the cases these causes were associated with one another. Among the less frequent conditions the author lists stones overlooked at the time of operation, strictures and obliteration of the deep biliary ducts, dyskinetic disturbance, the treatment of which is essentially conservative.

Because of multiplicity of factors the exact cause of a recurrence cannot be easily ascertained in most cases. Aspiration of duodenal contents, mineral waters, physical therapy, mud baths, a dietetic regimen, nupercaine hydrochloride blockade after Speranskiy, infiltration of Head's zones, and psychotherapy are the therapeutic measures first to be tried in the treatment of recurring manifestations

A secondary operation is indicated when conservative measures fail and when indications of a stone in the choledochus, of a stricture of a duct or of adhesions in the vicinity of the gastric antrum or the duodenum are present. The author concludes that the problem of prevention of recurrences after cholecystectomy depends on unanamity between surgeons and intermists as to operative indications. Only an early and timely operation is capable of further reducing the mortality rate and the incidence of failures

The Common Bile Duct

According to prevailing opinion, the function of the gall-bladder is to collect and concentrate bile, while the common duct is considered as a simple canal through which the bile flows toward the duodenum. However, Olvera A Acevedo³⁴ states that recent investigations

have shown that the common duct has the power of dilating or concentrating the bile and thus regulating the intracanalicular pressure. Of course, the sphincter of Oddi plays a great rôle in this regulatory mechanism. The common duct may be considered as a provisional warehouse for the bile, with a normal capacity of from 10 to 15 cc.

A dilatation of the common duct may occur in the course of an acute cholecystitis or as a result of visceromotor reflexes for which a duodenitis, periduodenitis, chronic pancreatitis, or carcinoma of the pancreas may be responsible. Finally, a dilatation of the common duct not infrequently develops after a cholecystectomy.

The prognosis and therapy of a dilatation of the common duct depend on its causative factors.

Surgical Treatment of Common Duct Stones

G H Copher³⁵ points out that the absence of pain in the presence of jaundice does not rule out the possibility of a stone in the common duct, as many patients with this condition have absolutely no pain during their illness

It is safer not to operate on a patient while the icterus index is rising, but to wait until the index maintains a constant level or is falling. The bleeding and clotting times of all patients with jaundice should be ascertained before operation. Patients with severe jaundice are very apt to bleed postoperatively in spite of normal bleeding and clotting times. Blood transfusions and glucose solution administered intravenously should be given preoperatively. Donors should be available during the operation and postoperatively in case additional transfusions are needed.

To palpate the common duct the author goes to the left side of the operating table.

In general, the indications for exploration of the common duct are: (1) A history of jaundice, chills, and fever; (2) a thickening and enlargement of the common duct, (3) thickening of the gall-bladder, and especially an associated thickening of the head of the pancreas, (4) the presence of many small stones in the gall-bladder and cystic duct, (5) the inability of the surgeon to determine whether obstructive jaundice is intrahepatic or extrahepatic in location, and finally, (6) the presence of definitely palpable stones in the common duct.

The duct is identified by aspiration with a fine needle. After exploration and removal of the stones from the common duct, the duct is irrigated with saline solution to wash out sand or small stones. The papilla of Vater is dilated mechanically The common duct is drained by a catheter introduced toward the hepatic ducts The author does not consider it necessary to gradually decompress the biliary system after relieving complete obstruction of the common duct.

The gall-bladder is not removed until after the surgery of the common duct is completed. The common duct catheter and a rubber dam drain are brought to the surface through a stab wound. The drain is removed in 4 days. The catheter in the common duct is usually removed in from 10 to 15 days except when there is pus in the drainage or if deep jaundice was present preoperatively.

If cholangiography is desired a 48 per cent solution of hippuran is preferred to heavy opaque oils for contrast material, as it is less likely to obscure small stones.

L. Gidro³⁶ does not consider it necessary to open the choledochus in all cases of lithiasis of the gall-bladder, but he is in favor of careful examination and frequent exploration by the sound. He recommends exploration by the sound

(1) if there are clinical symptoms of occlusion (icterus in the absence of occlusion), (2) if calculi can be palpated in the principal biliary passages, (3) if the choledochus is larger than ordinary, (4) if the choledochus or its surroundings show signs of inflammation, (5) if the cystic duct is so large that passage of the calculus into the choledochus is possible, (6) in cases of acute inflammation of the gall-bladder and (7) if the patient had icterus before he had pains. If the principal biliary passages are not detectable, it must be assumed that there are calculi in the choledochus In the latter case the author recommends retrograde exploration, that is, by way of the duodenum He does not open the choledochus during exploration but if possible enters the choledochus by way of the cystic duct. The result of the exploration of the choledochus determines the further surgical procedure

In case of negative results, after the cystic duct is cut, it is ligated or sutured and, unless the bile is not infected, cholecystectomy is performed. If calculi are found, it is not by choledochotomy but through the cystic duct with forceps and curet that the author removes the mobile biliary calculi, most of which do not exceed the size of a hazelnut. If the cystic duct is large enough, they can be made to glide out. The author employs this procedure more and more frequently During 1936-1937 he used it in 55 per cent of the cases of lithiasis of the choledochus. He used exploration by the cystic duct in 38 cases, and in 20 of these cases 1 or several choledochal calculi could be removed advantages of exploration and of lithectomy by way of the cystic duct consists on the one hand in making choledochotomy avoidable and on the other hand in being a more aseptic and a shorter operation than is choledochotomy.

That lithectomy by way of the cystic duct is not dangerous, the author demonstrates by citing the mortality rates of different operations: (1) Choledochotomy with drainage of the choledochus caused 6 deaths in 32 cases (mortality 1875 per cent). (2) Choledochotomy with primary suture of the choledochus (choledochorrhaphy) caused 4 deaths in 22 cases (18 per cent). (3) Exploration and lithectomy by way of the cystic duct (transcystic lithectomy) did not cause a single death in 38 cases. The author performs supraduodenal choledochotomy if exploration or lithectomy by the cystic duct is not possible and calculi are found in the hepatic canals He chooses retroduodenal choledochotomy if a calculus is found in the lower part of the choledochus or at the duodenal papilla. He resorts to transduodenal or intraduodenal choledochotomy if, because of adhesions and cicatrices, the choledochous cannot be found by other means drains the choledochus only in the following cases. If before or at the time of the operation there exists septic fever; if the bile contains much pus, if functional examination of the liver indicates grave parenchymal alterations, and finally if apart from the presence of choledochal calculi acute inflammation of the gallbladder exists

Detour Operations in Occlusion of the Biliary Tract

Detour operations on the biliary passages are necessary in cases in which complete occlusion of the biliary tract has resulted from pathological changes and cannot be corrected. The cause of such biliary-tract occlusions may vary and may be due to congenital atresia of the biliary passages, valve formation in the common bile duct with the formation of the so-called idiopathic choledochus cyst,

stenosis of the biliary passages as a result of inflammatory or traumatic changes or compression of the biliary passages from without by metastatic or tuberculous glands, or indurative processes in the head of the pancreas. W. Wagner³⁷ states that in these disease conditions. detour operations have stood the test of time. In recent years an attempt at extension of the indications for these operations has even been made, inasmuch as they have been recommended for multiple calculus formations in the biliary passages and in the presence of cholangitis However, these latter indications are not generally recognized as yet. Up to the present time there are relatively few reports on the results of such detour operations.

The author made a follow-up study of 36 such operations which included 26 cases of cholecystogastrostomy, 8 cases of cholecystoduodenostomy, 1 case of choledochoduodenostomy, and 1 case of choledochogastrostomy. In 14 of the 26 cases of the first group, a carcinoma of the head of the pancreas was present; in 5, a carcinoma of the papilla and common bile duct, and in 1, glandular metastases from a carcinoma of the tonsil. The remaining 6 cases were caused by benign compressions and stenoses. Three of the 8 cases in the second group were caused by a carcinoma of the head of the pancreas, of the common bile duct, and of the papilla, and the remaining 5 by benigh compressions and stenoses third and fourth groups presented a carcinoma of the head of the pancreas as the cause.

According to the reports in the literature, which are concerned mainly with choleduodenostomy, this method must be considered as the most useful and it is given preference by a number of investigators. The immediate results are very

good and the ultimate results are satisfactory also, even though, as is self-understood, they depend upon the basic disease, which is decisive for the subsequent duration of life. According to Heller and to Bernhard, the results of cholecystoduodenostomy and cholecystogastrostomy do not vary essentially, so that both of these procedures should be



Fig 13—The manometric equipment used in determining the pressure within the common duct. (Best, Hicken and Finlayson Ann Surg)

considered of equal value, an observation which the author believes he can confirm on the basis of his own little material.

There is no uniformity of opinion in the literature on the question of the occurrence of cholangitis. The only certainty is that the development of cholangitis occurs more often following an anastomosis between the hepatic duct and the gastrointestinal canal than with the use of the lower biliary tract and the gall-bladder. From the reports in the literature and according to the author's own investigations, the conclusion that the detour operations in occlusion of the biliary tract give good results both immediately and for a prolonged time is justified. With this method, both the pains

and symptoms of the patient, as well as the cholemia, may be overcome and a considerable prolongation of life, even in the presence of a malignant basis disease, may be achieved. The patient recovers his enjoyment of life and in a proportion of cases again becomes able to work. Consequently, the use of such detour operations can be recommended

patient to relieve such an obstruction, but during the last 18 months, R. R. Best, et al., 38 have been carrying out studies on the cholangiographic demonstration of such obstructing agents and a nonoperative method of removing them.

Fundamentally, the method they have used consists in increasing the pressure

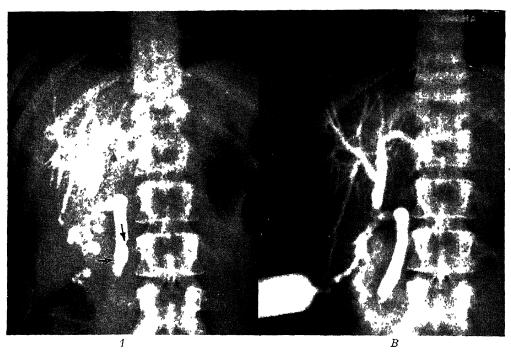


Fig. 14—(1) In this instance, the bihary fistula would not close and a cholangiogram revealed a filling detect at the lower end of the common duct. (B) After the described treatment, no foreign body was visible on the check-up cholangiogram and the fistula closed in 3 days (Best, Hicken and Finlayson. Ann. Surg.)

as being successful in cases of complete occlusion of the biliary tract that can be relieved in no other way

Effect of Dehydrocholic Acid Upon Biliary Pressure

Following cholecystectomy in some instances, symptoms develop which are referable to partial obstruction of the common duct, either by a calculus overlooked at the time of operation or by a mucous plug, blood clot, or inspissated bile. In the past it has been necessary on many occasions to re-operate upon the

behind the foreign body and relaxing the sphincter area in front of it, thereby permitting the object to pass out of the duct and into the duodenum, unless it is a stone of too large a caliber. There are 2 methods of increasing the pressure behind the obstructing agent. One depends upon the presence of a T-tube or catheter in the common duct and consists in irrigating the duct with sterile normal saline or other solutions, using a syringe to increase the pressure. The other method depends upon an increased flow of bile at an increased pressure in

response to a choleretic drug such as dehydrocholic acid.

The latter method has the distinct advantage that a fistula or drainage tube is not necessary, and it may, therefore, not only be applied as a therapeutic measure in all cases postoperatively, but may be used as an added step in the routine nonoperative management of gall-bladder disease. By employing de-

inspissated bile not infrequently inhibit the free flow of bile in the common duct and that even blood clots may be the source of obstruction. If these remain within the common duct, biliary symptoms persist or are aggravated and thus account for many of the poor results following cholecystectomies.

In the past, operative intervention was necessary or the patient's distress con-

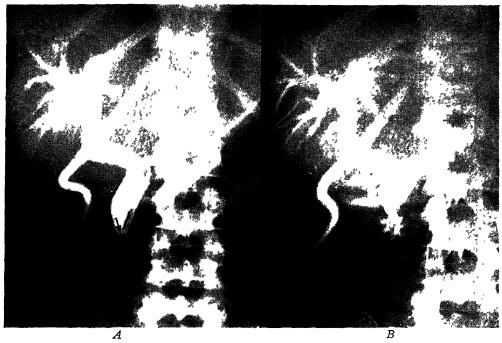


Fig. 15—(A) Postoperative cholanging ram revealed a stone remaining in the lower end of the common duct. (B) After several courses of treatment, cholanging ram shows that the stone has been dislodged from the common duct. (Best, Hicken and Finlayson. Ann. Surg.)

hydrocholic acid, the pressure may be exerted more or less continuously over a given period and at any momentary relaxation of the sphincter, autonomically, or through the use of drugs, the foreign body may escape from the duct

Clinical Application—As stated in the introductory paragraph of this article, the authors' experience with cholangiography have definitely proved to them that stones are not infrequently left within the common duct or are washed down from the liver into the common duct later; that plugs of mucus or tinued, unless nature expelled the foreign body from the duct. If the patient has a persistent biliary fistula or if a T-tube or catheter has been placed in the common duct, a definite picture of the obstruction may be obtained by injecting 10 to 25 cc of a sterile contrast medium, such as a 48 per cent solution of hippuran, into the tract or tube.

In most cases, the authors have been able to dislodge these foreign bodies by the following method, unless the obstructing agent was an exceedingly large stone. The pressure within the duct is

increased by giving 3 or 4 tablets of decholin (3\% grains-0.25 Gm.) or procholon 4 times a day for 3 days. On the first day, $\frac{1}{100}$ grain (0.65 mg.) nitroglycerin is dissolved under the tongue 3 times during the day, to relax the lower end of the common duct and permit the increased bile flow and pressure to flush out the duct. On the second day, atropine, $\frac{1}{100}$ to $\frac{1}{150}$ grain (0.65) to 0.45 mg), is given by mouth or hypodermically 3 times. On the third day, the nitroglycerin is repeated. Each morning before breakfast, during this 3-day regimen, the patient is given 1 to 2 drams (4 to 8 Gm) of magnesium sulfate in water and preceding the evening meal and at bedtime, 1 ounce (30 cc) of pure cream or olive oil, which also aids in relaxing the sphincter area at the lower end of the common duct.

During any momentary relaxation of the sphincter area afforded by these drugs, the increased intraductal pressure may force or flush the foreign body out of the common duct. If a T-tube is present or a biliary fistula exists, the common-duct is irrigated each day with sterile, warm normal salme solution followed by sterile, warm olive oil or warm iodized oil, such as lipiodol or lipiodine. The authors now keep the tube clamped or the fistulous tract packed for 2 to 3 hours following each administration of the nitroglycerin or atropine During the night, one may or may not keep the T-tube clamped, depending somewhat upon the degree of obstruction and the amount of pain ensuing This regimen is now used in all gallbladder cases postoperatively, and since common duct pathology is so common and possibly is the cause of distress in many cases of nonoperative biliary tract disease, it is also used in the medical management of this condition. authors have also proved that intrahepatic duct stones may be washed down from the liver by this method. Jaundice with complete obstruction of the common duct definitely contraindicates this method of treatment.

INTESTINES

Intestinal Obstruction

Incidence—Acute ileus occupied, according to S. S. Yudin,39 the fifth place among the acute abdominal infections treated at the Sklifasovsky Emergency Hospital. Thus during the period from 1928 to 1938 there were treated 6000 cases of acute appendicitis, 3500 of extrauterine pregnancies, 1400 perforations of the gastroduodenal ulceration, 1500 of incarcerated herma and 700 of acute intestinal obstruction. While the mortality rate was markedly lowered during this period for the first 4 forms of acute conditions within the abdomen, that of acute ileus still presented a mortality of 35 per cent as compared with the former figure of 50 per cent. The author emphasizes the diagnostic significance of the diminution of chlorides, while pointing out that its therapeutic value is somewhat limited. The postoperative prognostic value of the chloride curve is quite definite. Cases in which the chlorides continue to fall despite all measures invariably are fatal. If, however, the chlorides increase as the result of intravenous and subcutaneous introduction of salt solution, the chances for recovery in the gravest cases are much improved.

All the author's patients received 2 quarts (2000 cc.) of physiologic solution of sodium chloride before the operation and the same amount immediately after An additional 3 or 4 quarts (liters) are administered during the first 24 hours by means of the intravenous drip. The

author advocates *blood transfusion* of from 20 to 25 ounces (600 to 750 cc.) before the operation in order to combat shock, and another of similar amount after the operation in order to diminish the postoperative shock and to neutralize toxemia.

Etiology—Traumatic injury involving the abdomen directly, especially with injury to intra-abdominal organs or hemorrhage, may produce intestinal paralysis. K Lehmann⁴⁰ states that it is more difficult, however, to explain how extra-abdominal traumatic injury which is limited to the back, chest or pelvis can give rise to typical ileus. Some cases of serious paralytic ileus in traumatic injury to the back, including 1 with fatal outcome, gave rise to the studies here presented In order to get some idea of the frequency of this traumatic form of ileus, the author investigated a material of 497 cases of extra-abdominal traumatic injuries limited to the region of the back, chest, pelvis and kidney. In this number 11 were found to be associated with more or less pronounced paralytic ileus. One case terminated in death On the basis of the post-mortem observations in this case, of the localization of the trauma in other cases and of experimental studies, the author suggests that the intestinal paralysis is due to an inhibiting action on the intestinal musculature This effect is exerted by the sympathetic, which in turn is impaired by the formation of a hematoma. In 8 of the 11 reported cases the hematoma was localized in the region of the splanchnic nerves, more especially on their intrathoracic course

In the experience of J. W. Dulin and F. R. Peterson,⁴¹ intestinal obstruction due to gall-stones occurs with sufficient frequency to make it an important consideration in the diagnosis of acute abdominal conditions. This is particularly

true when the patient has previously had typical attacks of gall-stone colic. Also this type of obstruction may occur in a patient who has never had such an attack. The factors which make clinical diagnosis difficult are the similarity of the symptoms to those of an acute attack of gall-stone colic and the lack of early physical or laboratory studies which would positively indicate the nature of the condition. In the authors' series of 10 cases only 3 such diagnoses were made preoperatively. In 1 case a diagnosis depended on the disappearance of previously palpable stones in the gallbladder, in another a stone produced a negative filling defect in a flat teleroentgenogram The diagnosis was made in only 1 case which presented the classic history of previous biliary colic followed by a sudden development of symptoms of acute intestinal obstruction authors believe that greater awareness of this condition and the more frequent use of the teleroentgenogram will aid in making not only more frequent preoperative diagnoses but earlier ones While the teleroentgenogram may show only evidences of fluid levels within a dilated intestine, this observation is uncommon except when it is associated with paralytic ileus or mechanical obstruction

P N. Demidova⁴² states that the blood picture in 100 cases of incarcerated hermia showed during the first few hours, before the possibility of the development of dehydration, a moderate increase of the erythrocytes and hemoglobin. The author considers this erythrocytosis to be the result of reflex stimulation of the vegetative nervous system and the outflow of red cells from the reserve depots. This was accompanied by a mild leukocytosis with a moderate shift of the neutrophils to the left. She examined the blood picture in 158 cases of acute

intestinal obstruction. The blood picture here presented a marked increase in erythrocytes up to 6,000,000 and a correspondingly high hemoglobin, up to 120 per cent, a leukocytosis of from 12,000 to 30,000 a neutrophil shift to the left, hypoeosinophilia and, in a number of cases, inonocytosis. A more detailed analysis showed certain differences in different types of obstructions.

Obstruction of the sigmoid in 25 cases presented a mild erythrocytosis with a mild leukocytosis (from 9000 to 15,000), with a moderate shift of the neutrophils to the left, a picture resembling that of the early incarcerated hernia and suggesting absence of toxemia. Hens of the small intestine in 25 cases presented a blood picture with a marked increase of the erythrocytes up to 6,000,000, a leukocyte count up to 23,000 and a marked shift to the left of the neutrophils with the appearance in some cases of immature cells and of myelocytes. The leukocytosis in these toxic cases is soon replaced by leukopenia. The author concludes that the blood picture in ileus has a diagnostic value in reflecting the 3 stages—that of initial pain and irritation of the vegetative nervous system, that of intoxication, dehydration and thickening of the blood and that of intoxication and beginning infection (peritoritis)

Pathological Physiology — Numerous attempts have been made in the past to ascribe the disastrous effects of all types of intestinal obstruction to some one etiological factor. Of the numerous explanations offered, II G Scott⁴³ shows that intestinal toxemia has been given the greatest consideration. Hundreds of investigators have attempted to put the blame on this or that toxin as being directly responsible for the directly results. There was never at any time any agreement as to what toxin was responsible. Moreover, the fact that no

theory of intestinal toxemia has ever offered any benefit to the patient in the way of improved methods of treatment or lowered mortality has cast grave doubt on this explanation. However, so firmly has the theory of intestinal toxemia become rooted in the consciousness of medical practitioners that the concepts advanced in more recent years have been but slowly and hesitatingly accepted.

During the past 30 years investigators have shown, anatomically and pathologically at least, that intestinal obstruction may be divided into 2 major types, or a combination of the 2 Clinicians and investigators alike have used the terms "simple obstruction" and "strangulation obstruction" to designate and differentiate the 2 major forms. Of recent years such investigators as Wilkie, Murphy, Elman, Scott, Blalock and Mensing have called attention to the fact that the loss of blood in intestinal strangulation may be of some consequence in bringing about and aggravating symptoms of shock and in causing death. Wilkie, in 1913, clearly distinguished between simple and strangulation obstruction was impressed with the amount of blood lost in strangulation obstruction and believed that it played an important rôle in the causation of shock and death While conducting some experiments on strangulation obstruction in the dog, the author observed significant loss of blood into the walls and lumen of the strangulated bowel. The present paper by the author is the outcome of further experiments which he conducted in order to determine the extent of the loss of blood and its relation to changes in the blood pressure, shock, and death as seen in these conditions. In this paper the results of 240 experimental strangulation obstructions are presented

Before proceeding with the subject matter of these experiments, it might be

well to refer briefly to the terminology used. The term "simple obstruction" refers to the occlusion of the lumen of the bowel without gross interference with the mural blood supply. The term "strangulation obstruction" implies a vascular impairment of the wall of the bowel and its mesentery. The author points out that at operation or autopsy, patients for whom the diagnosis was made clinically not infrequently showed some evidence of both types of obstruc-Most strangulation obstructions are accompanied by a simple mechanical or neurogenic obstruction. Because of a rather frequent combination of simple and strangulation types, with their overlapping syndromes, many patients observed clinically fail to present typical symptoms of either type of obstruction Consequently, the surgeon and clinician find it rather difficult to realize that 2 entirely different physiopathological processes might be responsible for producing the many complex effects of intestinal obstruction

The author ingeniously employed 4 methods in producing the experimental strangulation obstructions recorded in this paper, in order to make it possible to evaluate the rôle that the arteries and vems may play, individually and collectively, in determining the period of survival of dogs with strangulation obstruction In his first method a partial occlusion of lumen and blood supply was employed. This group represented obstruction by encirclement only. In the second, there was complete arteriovenous obstruction. The third featured complete arterial obstruction with a patent vein, while the fourth featured complete venous occlusion with an intact artery These 4 methods make possible an interesting comparative study.

The author gives a detailed account of the pathological and microscopical

findings of each group and lists the results in tabulated form. Naturally, marked differences were noted in the various groups. The gross pathological picture, as well as the microscopic observations in all instances, however, indicated a loss of whole blood in the wall and lumen of the strangulated loop of the bowel. It was found that the relative degree of venous or arterial occlusion determined the type of strangulation produced. With venous occlusion predominating, the loss of whole blood was the chief factor. With arterial occlusion predominating, the loss of plasma was important.

Increase in the weight of the strangulated bowel over the normal weight was likewise observed by the author. This increase in weight was shown to be due to the accumulation of blood in the wall and lumen of the strangulated loop of the bowel. Further observations showed that the hemoglobin content of the material within the loop was high and that the free peritoneal fluid was similar in total protein content to the animal's own blood plasma.

The author was able to calculate the loss of blood in strangulation obstructions. This loss of blood, in the venous types of occlusion at least, was found adequate to account for the shock and death of the experimental animal. Experiments in these instances tended to show that the blood pressure falls rapidly and the hemoglobin content drops rather uniformly.

Furthermore, the author established the fact that there was a definite correlation between the fall in the blood pressure and the time, length, and type of intestinal strangulation. In general, the longer the time and the longer the loop strangulated, the greater was the fall in the blood pressure. The type of obstruction, however, was of even greater im-

portance. In those instances in which the veins alone were ligated, and in the strangulations involving encirclement in which the arteries were not entirely occluded, the fall in pressure was much more rapid than in those instances in which the arteries were absolutely occluded, with or without occlusion of the veins.

Additional experiments were presented to demonstrate that "toxic products" are not present in the peritoneal fluid except terminally when the loops are gangrenous or ruptured In view of the controversy concerning the absorption of so-called "toxic products" from the obstructed bowel, it was deemed advisable to test the absorptive power of the normal and of the strangulated intestine for products of known toxicity. Histamine, strychnine, and tetanus toxin were introduced into strangulated loops (the usual 4 types of strangulation were employed) in order to test the absorption of these products. Careful experiments were carried out to make a complete check-up from this angle. Practically all the tests failed to reveal any evidence of absorption of these products, except terminally, when the loops were gangrenous or ruptured

Later experiments were carried out which tended to show that the intestinal wall per se is not toxic. In order to determine whether the wall of the bowel itself was "toxic," an attempt was made to free the normal intestine of the dog from its usual bacterial flora by chemical and thermal sterilization. Segments of bowel thus treated were placed in the peritoneal cavities of normal dogs, in order to determine their relative and actual degree of "toxicity," as judged from a clinico-experimental standpoint. These experiments substantiated the experimental results of other investigators.

notably Dragstedt and his co-workers. who showed that it was extremely difficult to sterilize the normal bowel with the usual antiseptics. Careful bacteriological studies were then conducted and these tended to show that the only evidence of toxic absorption was found late in the course of any strangulation obstruction and was apparently due to the presence of innumerable bacteria in the peritoneal cavity. The author observed that the effect of the bacteria was apparently quantitative, as gross perforation of the intestine was essential to a lethal issue when the peritoneal fluid was tested by introducing it into the peritoneal cavity of a normal animal.

The author draws some interesting conclusions from his experiments which are of great significance. In the first place, strangulation obstruction, like intestinal obstruction in general, is not a distinct disease. To quote the author. "The train of symptoms, the development of shock and finally the ensuing death depend on at least 3 factors:

- "I Loss of blood into the wall of the bowel, the lumen, and the peritoneal cavity
- "2 Transudation of plasma into the general peritoneal cavity
 - "3 Absorption of bacterial toxins

"The course taken in any strangulation will depend on the relative degree of venous or arterial occlusion. If arterial occlusion predominates, the resulting pathological picture will be an anemic or hemorrhagic necrosis without marked distention of the lumen or the wall of the bowel. In these instances there will be an outpouring of plasma from the surrounding peritoneal surfaces in an attempt to rid the peritoneum of the gangrenous bowel. Death will occur relatively late and will be secondary to a loss of plasma into the peritoneal cavity

and an absorption of bacterial toxins therefrom. If, on the other hand, the venous occlusion predominates in the face of normally patent, pumping arteries, or even partially patent arteries, the result will be a loss of whole blood into the wall and lumen of the bowel and a transudation of plasma into the peritoneal cavity, associated with a distention of the strangulated loop, varying from a moderate to a marked degree "

From these observations it seems quite plausible to add that whole blood and plasma are apparently lost from the general circulation in quantities sufficient in themselves to account for the symptoms of shock and death which occur in most cases of strangulation obstruction.

J. Bottin⁴⁴ believes that the cause of death in obstruction of the upper portion of the small intestine is primarily intoxi-Even though dehydration and cation demineralization are common in obstruction of the upper portion of the small intestine, they are far from being constant or constantly acute; even if these conditions are corrected, death is delayed in the majority of cases only for an insignificant period. Clinical and laboratory conditions associated with much more marked demineralization and dehydration than noted in high obstruction of the intestine do not usually lead to a fatal termination; if death does ensue, it occurs at a much later period. These facts do not diminish the importance of the factors of dehydration and demineraliza-Rehydration and remmeralization may prevent death, due to high intestinal obstruction, in more animals than exclusion of the pancreas, but the results are much more inconstant and irregular. The author has performed many experiments with exclusion of the pancreas. He concludes that high intestinal obstruction as well as low obstruction of the small intestines leads to an intoxication, which represents the primary cause of death. The course of the disease depends not upon the existence of dehydration or demineralization but upon the distance of the obstruction from the duodenopancreatic tract.

The distention factor in simple intestinal obstruction has been studied by O. H. Wangensteen and C. E. Rea.⁴⁵ The demonstration of the possibility of relief of certain mechanical obstructions by suction applied to an inlying duodenal tube supports the belief that distention with its associated sequelae was the item of chief importance in causing death in ileal obstruction. The agents causing the distention are gas and the digestive juices. McIver and his associates have shown swallowed air to be the principal source of gaseous distention of the stomach after abdominal operations In this laboratory it has been shown that swallowed air accounts for about 68 per cent of the gas present in instances of simple mechanical obstruction. Having in mind the great absorptive capacity of the small intestine, it is quite reasonable to assume that, if swallowed air could be excluded from the intestine even in the presence of obstruction, the digestive juices could be absorbed and obstruction of the terminal ileum tolerated fairly well

A method of exclusion of swallowed air from the intestine by cervical esophagostomy was performed in dogs by a 2-stage operative procedure. In 11 such dogs the average survival period after the establishment of complete occlusion of the terminal ileum amounted to 36 days. One of the animals survived for a period of 57 days. The authors found that dogs in which a long closed loop of esophagus, stomach, and entire small intestine was made absorbed the digestive juices when swallowed air was excluded.

At autopsy the gut was usually found collapsed. The exclusion of swallowed air obviates the distention factor. It also relieves the sequelae of decreased viability and increased permeability which attend sustained increases of intraluminal pressure.

The experiments indicate that complete occlusion of the terminal ileum may Wangensteen⁴⁶ states that only strangulating obstructions and obstructions secondary to an inflammatory condition show tenderness and rigidity. X-rays of the abdomen are useful in the demonstration of gas in the bowel and in localization of the obstruction in the small bowel or colon. Occasionally barium must be administered to localize the proc-

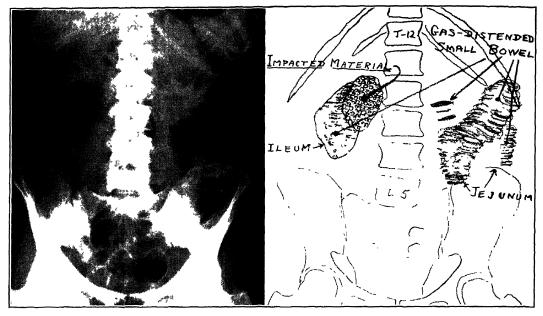


Fig 16—Case I Mis S E, aged 39 years, vential projection of the abdomen with patient prone. Note the distended small intestine outlined by gas, the jejunum on the left side of the abdomen showing well-marked valvulae conniventes, the large loop of ileum in the right side of the abdomen identified by the lack of mucosal folds. The patient had a laparotomy 3 years ago and adhesions are responsible for the present obstruction. They have been present for a long time, without clinical evidence, and the immediate precipitating cause of symptoms is visualized in the roentgenogram and is apparently a large piece of some undigested material, impacted at the site of an adhesion. When this film was made the patient was in great distress, with all the signs and symptoms of intestinal obstruction, (Chamberlain, S Clin North America, W B. Saunders Co., Philadelphia.)

be well tolerated if the gut is not allowed to become distended by swallowed air. In effect, the experiments indicate that the mechanical factor of distention and not a "toxic factor" accounts for the lethal issue in ileal obstructions.

Diagnosis—Of all abdominal colics, only intestinal obstruction is characterized by recurrent intestinal borborygmi as the acme of concurrent crampy, colicky pains of short duration. O. H.

ess accurately Vonnting is characteristic of obstruction of the small bowel. It is uncommon or occurs late in colon obstruction, in which condition the competent ileocecal valve prevents this symptom. Persistence of gas in the colon after evacuant enemas, with a relatively mildly distended small bowel, upon x-ray examination suggests partial occlusion, while the absence of gas in the colon under such circumstances points to a complete

obstruction. The diameter of the colon has been found to be the best guide as to the degree of its obstruction.

The general effects of intestinal obstruction are dehydration, dechlorination, and loss of blood, the same as in strangulating obstructions. The effect on the bowel wall is a gradual compression of the vessels in the wall by increased in-

early cases of obstruction which the clinician may not be able to do even after thorough examination. Ochsner proved that strangulated obstruction can be demonstrated with x-rays after 1 hour, and simple obstruction after 3 hours. He concluded that an accumulation of gas is the first sign rather than an accumulation of gas and fluid. In all suspected cases of

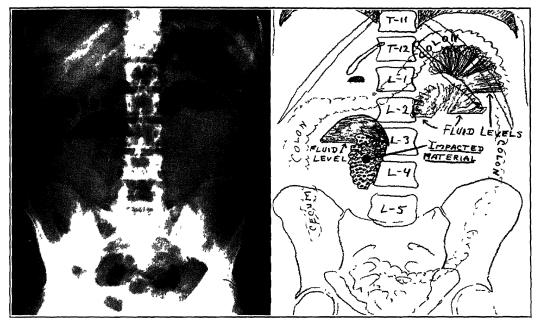


Fig 17—Case I Ventral projection with patient sitting. Because the beam of x-rays was horizontal, fluid levels are visualized in the distended loops of obstructed small intestine. The actual point of obstruction is visualized in these films where the mass of undigested material is lodged, in the caudal end of a gas-distended loop of ileum, at the right border of the shadows of lumbar vertebrae L-3 and L-4. Such a film as this one immediately placed the obstruction in the ileum and not in any part of the colon. Had it not been for the availability of the Miller-Abbott tube, this patient would have needed immediate operation. (Chamberlain S. Clin. North America, W. B. Saunders Co., Philadelphia.)

traluminal pressure until the wall becomes permeable to organisms lying in the lumen. Sustained increases in intraluminal pressure can occasionally lead to perforation in the colon because of the usual competence of the ileocecal valve. This rarely occurs in the small bowel because of the decompression that is produced by vomiting.

X-rays in Diagnosis—L. Solis-Cohen and S. Levine⁴⁷ believe that the radiologist can make a correct diagnosis in

ileus the authors routinely take 3 views, the anteroposterior, the posteroanterior, and the upright They believe that the anteroposterior view is the most valuable for the differentiation of the large bowel from the small

The first x-ray signs in an incipient case of ileus of mechanical origin are the presence of trapped gas and what is termed the "hairpin turn" The persistent appearance of a dilated loop of small bowel on successive films at hourly inter-

vals is, in the opinion of the authors, evidence of an oncoming ileus A dilated "hairpin turn" in the small bowel is the beginning of the so-called "stepladder appearance," and in its presence a developing ileus must be suspected.

The significance of intestinal gas within both the small intestine and colon is as follows: If the entire colon is dilated and Morphine produces a general atonicity of the intestinal tract, and its effects may be manifested by large accumulations of gas, both in the colon and in the small bowel. The distribution of gas permits the differentiation of morphinization from ileus.

Fluid levels in the obstructed bowel are apparently late signs of obstruction

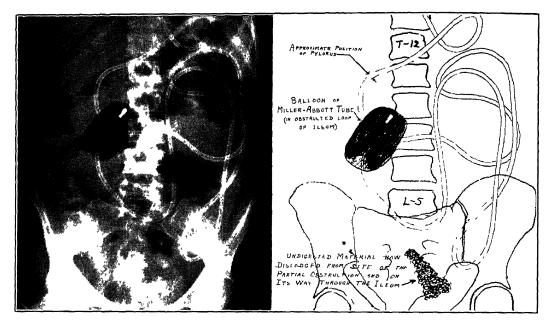


Fig. 18—Case 1. Ventral projection with patient sitting, after passage of the Miller-Abbott tube. The balloon was left uninflated until fluoroscopy showed the advancing head of the tube in the descending portion of the duodenum. Progress to that point was slow and required about 1 hour, with a certain amount of manipulation under fluoroscopic guidance, to hasten the passage of the pylorus. After distention of the balloon, progress was very rapid. The principal lumen of the Miller-Abbott tube was kept connected to Wangensteen suction apparatus. When the measuring marks on the Miller-Abbott tube showed a distance of 3 text beyond the pylorus, the patient became perfectly confortable. By this time all gas collections in the small intestine had disappeared except the collection of air in the distended balloon of the Miller-Abbott tube. About 2 pints of corrosive, odorous, brownish liquid had been recovered through the principal lumen of the tube. Note the shadow of the obstructive material, apparently dislodged from the obstructed loop of the ileum. (Chamberlain, S. Clin, North America, W. B. Saunders Co., Philadelphia.)

only a small amount of air is seen in the small bowel, obstruction of the small intestine can be excluded. Tremendous dilatation of the colon, or a part of it, associated with fluid levels and the absence of gas in the small intestine is indicative of obstruction of the large intestine. It is sometimes difficult to differentiate between the large and small bowel.

and are due to intestinal hypersecretion. The higher the obstruction is situated, the greater the amount of fluid present. Marked distention of loops of the small bowel points to a high obstruction. The typical "stepladder appearance" is a late sign of obstruction. The presence of striations in the mucosa indicates jejunal obstruction, while the ileum is relatively free of valvulae conniventes. Duodenal

or jejunal obstruction due to subhepatic collections is typified by marked distention of proximal loops of the small intestine and gastric dilation.

The differentiation of adynamic ileus, peritonitis, and mechanical obstruction may be impossible by roentgenography

is high or low, most often he cannot state definitely in which quadrant of the abdomen the lesion is situated.

In commenting on roentgenologic aids in the diagnosis and management of intestinal obstruction. W. E. Chamberlain⁴⁸ states that "scout films" (roent-

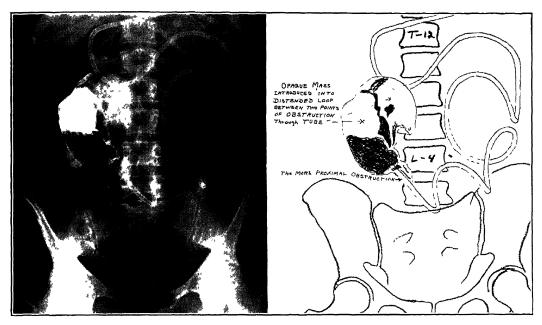


Fig 19—Case I Vential projection 24 hours after Figs 16, 17 and 18, patient prone. As long as the Miller-Abbott tube remains in situ, the patient can be allowed unlimited fluids and selected nutriment. At the time of the making of this roentgenogram, the distal end of the tube was but 3 feet past the pylorus, yet it was very near the ileocecal valve (subsequent operative finding). In the present case, the length of tube beyond the pylorus varied from 3 feet to 5 feet, but regardless of this measurement the distal end of the tube was seen to remain in the same loop of ileum, between the 2 constricting bands indicated in the diagrams. Dissecting room studies give an entirely erroneous impression concerning the length of the small intestine. During life the length of the small intestine varies from hour to hour, and the variability is so great that the Miller-Abbott tube has frequently reached the cecum in normal subjects when as little as 4 ffeet past the pylorus. Even shorter measurements have been obtained. The barrum which is visualized in the present roentgenogram was administered through the principal lumen of the Miller-Abbott tube. The more proximal obstruction is quite thoroughly visualized. The more distal obstruction is indicated but not visualized. (Chamberlain, S. Clin. North America, W. B. Saunders Co., Philadelphia.)

alone Dynamic ileus is diffuse and generalized and usually presents marked dilatation of the bowel Carcinomatosis has been diagnosed roentgenologically by the observation of features of obstruction with a generalized haze throughout the abdomen, coupled with fading or complete blotting out of psoas shadows.

While the roentgenologist may venture an opinion as to whether the obstruction genograms made without the administration of opaque media, or any other special preparation of the patient) are often of great value in cases of suspected, or known, bowel obstruction or ileus. Frequently such film studies will locate the obstruction and reveal its nature. In cases where rupture of a hollow viscus has occurred, the film may reveal the condition by visualizing the abnormal

gas content of the peritoneal cavity, particularly if the film was made with a horizontal x-ray beam.

The use of the Miller-Abbott tube will enable the surgeon to prepare a case of small bowel obstruction for operation by intubation and drainage of the obstructed segment. The author shows

large quantities, and with simple ions, particularly chlorine, sodium, potassium, and calcium, in an isotonic or mildly hypertonic solution. Local or regional anesthesia is best, but spinal anesthesia may be indicated in certain cases

An essential of the surgical treatment of intestinal obstruction is always to prac-



Fig 20—Case I Roentgenogram 48 hours after legs 16, 17 and 18, patient sitting Approximately halt of the barium has passed the obstruction and is distributed along the colon. The patient remains clinically well, except that she complains of soreness in her throat where the tube irritates the mucosa. Shortly after the making of this roentgenogram, the Miller-Abbott tube was removed. This was accomplished by deflating the balloon, withdrawing the tube gently until resistance was encountered, and then anchoring the tube and waiting 10 minutes or more for additional "slack" to develop. By repeating this procedure at intervals of 10 to 15 minutes, the tube was recovered in about 40 minutes, without inconvenience to the patient. (Chamberlam S. Clin North America, W. B. Saunders Co., Philadelphia.)

that the active co-operation of the radiologist is needed for the successful application of the Miller-Abbott method to the clinical problem of small bowel obstruction

Treatment—Certain principles in the treatment of intestinal obstruction are fundamental. If the patient's condition is not too grave, it may be advisable to postpone operation for several hours in order to restore water and minerals that have been lost. This treatment consists in furnishing the body with water in

tice the simplest kind of procedure J Bottm⁴⁹ points out that it is obstruction that must always be treated. It alone constitutes the emergency. The aim of all treatment is to remove the obstruction by the simplest means. Experience teaches that frequently a simple operation will save a life and will permit later and safer treatment of the causative lesion. A complicated operation may relieve the obstruction, but will result in a large number of fatalities. If one attempts resection and suture of the ob-

structed bowel, one must expect some disagreeable complications to ensue. No tissue is less suitable for suture than the obstructed bowel.

The postoperative treatment is most important. *Rehydration* and *remineralization* must be accomplished by means of fusions or injections of large amounts of

common conditions are those resulting in partial or complete obstruction, but excessive peristalsis and diarrhea also express relative incompetency. He refers to certain reflex gastrointestinal arcs, such as the ileopyloric reflex, in which irritation about the ileocecal valve results in pylorospasm, consequent gastric reten-

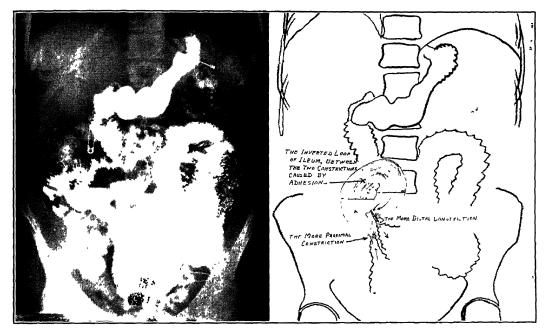


Fig 21—Case I Ventral projection 5 days after passage of Miller-Abbott tube and 3 days after removal of same Barium administered by mouth reveals normal stomach and duodenum, and a normal small intestine down to the points of obstruction in the ileum, previously demonstrated. At operation 3 weeks later, the findings were exactly as demonstrated in this roentgenogram. A somewhat dilated loop of ileum, inverted, constituted a sort of volvulus between points of narrowing, caused by adhesions to the ventral abdominal wall. As shown by the earlier roentgenograms, it was into this loop of ileum that the balloon of the Miller-Abbott tube became inserted. The balloon passed the proximal obstruction, but never passed through the distal obstruction (Chamberlain S Clin North America, W B Saunders Co, Philadelphia)

isotonic, or mildly hypertonic, solutions of chloride, sodium, potassium, and calcium *Gastric lavage* or, better, *duodenal suction* by the Wangensteen method is excellent for removing the toxic material from the stomach and small bowel

The prevention and management of postoperative intestinal incompetence is outlined by W. W. Babcock.⁵⁰ By intestinal incompetence the author refers to inadequate motor, secretory, or absorptive capacity of the bowel. Obviously, the

tion, and accumulative hyperchlorhydria Familiarity with the gastrointestinal expressions of cardiovascular, pulmonary, renal, or pelvic disease, as well as of tabes, herpes, psychoneurosis, hyperthyroidism, plumbism, and the like, may prevent serious errors in diagnosis and treatment. Babcock believes that drastic purgatives and repeated enemas, which have been used for many years, preceding the operation, as well as the calomel and saline laxative administered after the

operation, have created much postoperative voniting, cramps, and tympany. He does not believe that the various drugs injected subcutaneously to stimulate the laggard bowel, such as strychnine and eserine, are of any value.

After the exposure and trauma of an abdominal operation, 2 or 3 days of rest

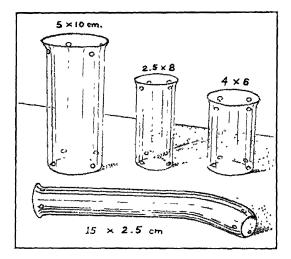


Fig 22—"Lamp chimney" or large caliber tube drains of nonsoluble glass provide prolonged and adequate drainage and a means for internal exteriorization. The perforations enable anchoring of the drain with 4 fine wire sutures. The long tube is used for the prostatic bed. A similar tube with small perforations is used to drain the pelvis through the perineum or vagina.

usually are required for the gut to regain its normal function. During this period aggressive stimulation is harmful. Laxatives may provoke vomiting and distention, and enemas are usually ineffective and cause discomfort. If a rectal tube is used, it should be a well lubricated small catheter. Babcock believes that as long as inadequate attention is given to the avoidable causes of postoperative intestinal incompetence, it is evident that the temptation to use peristaltic tonics will recur. If used, they should be used with much circumspection, and never if there is peritonitis or organic obstruction.

The author has seen patients in whom the appendiceal stump was blown out,

and perforating ulcers of the intestine have been observed in patients in whom such injections were used. Unnecessary and unanatomical incisions, while not so common as formerly, are still observed. Instead of excising an old scar with its defects and adhesions, the operator makes a new one with a new line of denuded tissue to fuse with underlying intestinal structures. Babcock believes that if the peritoneal tears and the muscle come in contact with bowel, an important source of adhesions is left Such peritoneal separation is most easily prevented by transverse or oblique incisions. He does not believe in the use of amniotic fluid or ferments as a routine treatment for the prevention of peritoneal adhesions Retained blood and clots in the peritoneal cavity provide culture media for bacteria and a matrix for organized adhesions Suture and ligature material may produce a decided reaction in the wound This is true particularly of catgut to which some persons may be susceptible, while wounds sutured with silk, or rustless steel wire heal more rapidly, with greater strength, and less tissue reaction

The author decries the use of rubber and gauze drains. He prefers nonsoluble, pyrex glass of large diameter, to which there is little plastic reaction glass tubes from $2\frac{1}{2}$ to 5 cm in diameter, which he calls "lamp chimney drains," are anchored to the wound but float in the peritoneum. He believes that swallowed air is the chief ingredient of gases present in the gastrointestinal tract during the postoperative period. Persistent eructation should be treated by suction drainage or an anchored cork between the teeth He believes that most patients do far better if visitors and sympathetic members of the family are not permitted to see them Fruit juices, fats, coarse foods, and those to which the patient is

allergic should be avoided. Asafetida rectal suppositories, and small enemas of the milk of asafetida have some value in the prevention of colonic distention. The Wangensteen type of gastroduodenal suction is advantageous in postoperative ileus, but the Miller-Abbott tube should be reserved for a few special cases. Babcock by far prefers multiple enterostomies and colostomies in the presence of ileus from peritonitis. He believes that enterostomy is perhaps the most useful operation for postoperative ileus. For the performance of the enterostomies, he uses evipal combined with local anesthesia.

Regional Ileitis

C. G. Mixter and A. Starr⁵¹ have studied and treated 20 cases of regional ileitis. The disease is essentially one of youth Eleven of the authors' patients were under 25 and 7 were between 25 and 35 years of age The *etiology* of the disease still is uncertain. The lesion most often involves the terminal ileum, stopping abruptly at the ileocecal valve, where the process shows its greatest activity. The disease is progressive, lasts for months or years, and tends to fall into 4 phases.

The first stage is that of an acute intraabdominal lesion with evidences of peritoneal irritation. Acute pain in the right lower quadrant, vomiting, fever, leukocytosis, and abdominal tenderness and spasm may be present. The disease in this stage resembles acute appendicitis. At operation, an excess of free peritoneal fluid is found and the terminal ileum is reddened and thickened. Invariably enlarged mesenteric glands are seen

As the disease advances (second stage), the symptoms are those of mild idiopathic ulcerative colitis, i. c, frequent loose bowel movements, recurrent bouts of fever, cramplike abdominal pain, pro-

gressive weakness, and loss of weight; but there is no tenesmus. Lower abdominal tenderness usually is present, and a mass may be palpated by abdominal or rectal examination. Proctoscopy fails to show the usual lesions of ulcerative colitis in the lower bowel. Anemia and leukocytoses are common At operation the terminal ileum is thickened and edematous, with corresponding involvement of the mesenteric lymph glands. Many ulcerations are found in the mucosa of the diseased bowel.

The third stage is that of chronic partial intestinal obstruction as the result of extreme thickening of the wall of the bowel and scar formation from the healing of the mucosal ulcerations. The constriction is most marked near the ileocecal valve Severe cramps, nausea, vomiting, and constipation are frequent complaints A mass is almost always palpable at this stage.

The fourth stage is characterized by the development of multiple sinuses and fistulas between various loops of bowel and between the bowel and the outside. These result from slow perforation of the mucosal ulcers. The diseased bowel and its mesentery are enormously thickened and doughy Walled-off abscesses between adjacent loops of bowel are common Fecal fistulas are frequent and resist all efforts at closure until resection of the diseased bowel is carried out

The diagnosis of regional ileitis should be considered whenever a young adult complains of symptoms suggestive of partial intestinal obstruction, particularly if there is evidence of an associated low-grade inflammatory process. A history of colicky abdominal pain and irregular bowel habits, together with loss of weight, slight fever, leukocytosis, and anemia, are highly suggestive. The finding of a palpable mass is important additional evidence. In the later stages of the disease,

x-ray examination reveals a filling defect in the terminal ileum with stasis and distention proximal to it. In cases in which the stenosis is marked, the lumen appears as a fine line of barium, the so-called "string-sign" of Kantor.

Treatment depends upon the stage of the disease and the condition of the patient. In the advanced cases, surgical extirpation is indicated. The hazards attendant upon radical surgical procedures are peritonitis and sepsis resulting from the activation of latent infection as the result of operative manipulation In the opinion of the authors, resection of the involved bowel in 1 or more stages seems at present to be the best form of treatment. When obstructive symptoms, fistulas, or abscesses are present, graded procedures such as drainage of the abscess followed by ileocolostomy and subsequent resection sometimes are advisable. The authors' best results have been obtained in cases in which a 1-stage ileocecal resection could be performed and the abdomen closed without drainage. They observed no case in which cure was accomplished without resection of the bowel.

Diverticulosis and Diverticulitis of the Colon

According to T. Stenholm, ⁵² one should speak of diverticulosis only in the presence of a simple, noninflanied herma of the bowel. These hermas are often observed as an incidental finding in a routine x-ray examination. Only with the occurrence of inflammatory signs is a definite picture of clinical importance observed. Diverticula are rare before the fortieth year of life, and men are affected twice as often as women. The diverticula may occur at any point along the colon, but the sigmoid is the commonest. The causes of the formation of diverticula may be the weakness of the musculature.

of the bowel wall, unusually wide vessel spaces, nervous influences, and, especially, increased intraluminal pressure. as, for instance, in chronic constipation If inflammatory signs are superimposed. one refers to the condition as diverticulitis. The course is often very rapid with purulent degeneration, necrosis, or perforation Formes frustes perforations are possible, as well as perforations into neighboring organs, as, for instance, the bladder, and fistula formation. The diverticulitis may cause a narrowing of the left ureter and thus a hydronephrosis, as well as a purulent phlebitis of the inferior mesenteric vein There is no definite proof of connection between diverticulitis and carcinoma Only Clairmont has reported a case in which these 2 conditions were present

The clinical and diagnostic signs are uncertain Inflammation in the vermiform appendix, peptic ulcer, and inflammation in the adnexa must be differen-The author reports 1 case in which a perforated diverticulum resulted in peritonitis. If the course is more chronic, one must differentiate colitis. If there is a marked inflammatory tumor, carcinoma must be differentiated, although this can be more easily done from the previous history. The symptoms are of long standing in diverticulitis, and the patient does not have cachexia or blood in the stool. The inflammatory tumor is usually not as hard as in carcinoma. One cannot, however, rely too much upon these signs. Often the roentgenogram may give definite help. It is absolutely necessary that the bowel be cleaned well By the administration of atropine before the roentgenogram is taken the small herniations are made more visible. The injection of air as described by Fischer often is of help. Because of the inflammatory changes in the wall of the bowel, filling defects can be observed and easily

be taken for a neoplasm. Nevertheless, these inflammatory defects are usually more extensive than in carcinoma. The mucosa, however, is unchanged as can be seen in the mucosa relief film. The examination with the x-rays is not entirely without danger, as perforation may occur. The same danger also obtains for proctoscopy, which is worthless as the diverticular openings are usually shut by swelling.

The treatment formerly was entirely surgical, although medical treatment helped a great deal, as is illustrated in a case The simplest procedure is a simple colostomy, which permits putting the bowel at rest and regular irrigations. In 1 patient a good result was obtained by this procedure. If there is a question of perforation, it is usually best to await a The acute symptom usually remission disappears rapidly Should operation be necessary, the closure of the perforation is often difficult because of the inflammatory changes in the wall of the bowel It is often impossible to avoid tamponade and temporary colostomy. Abscesses should be simply drained. If ileus symptoms are prominent, then colostomy or cecostomy must be performed It is important to clear the findings when carcinoma is suspected. A more radical procedure is the exterioration as described by von Mikuliez with secondary resection. The author advises against such a procedure in the acute stages Resection should be attempted only rarely as often the entire colon is affected; if it should be necessary, it should be done in 2 stages Transversosigmoidostomy is recommended. Sudek has advised sounding of the stenosis from the colostomy opening. With this the danger of perforation is great. When repair of a fistula between the bladder and colon is made a colostomy is always necessary. Lauber reports an operative mortality of

40 per cent and Gerzowitsch reports good results in 50 per cent.

Late Results in Diverticulitis—An analysis of the results obtained in the treatment of 136 cases of diverticulitis is presented by J. P. Lockhart-Mummery.⁵³ Ninety-one of the author's patients were treated by operation. There were 15 deaths, i. e., a mortality of about 10 per cent of all the cases. In 13 patients the involved portion of the colon was freed from other structures, and omentum was wrapped around it and held in position with fine catgut sutures. A colostomy, usually in the transverse colon, was carried out in the cases of 38 patients. The author believes this to be the most satisfactory type of treatment and the safest method of dealing with severe cases of diverticulitis which do not respond to medical treatment. In 17 patients, the diseased portion of intestines was resected, with temporary cecostomy or colostomy. The artificial anus should remain at least 1 year, or until all signs of sepsis have disappeared This is advocated as the ideal treatment when the area involved is small.

Exploratory laparotomy was performed in 43 patients. In this group were many cases of acute perforation with abscess formation which could only be drained In 2 of the patients, carcinoma developed in the sinus tract. Appendicostomy was carried out in the cases of 5 patients who failed to respond to medical treatment This procedure may be used instead of colostomy Twelve patients developed a vesicocolic fistula. In only 1 instance, however, was this responsible for a fatal pyelitis All 12 patients were treated by colostomy followed by resection of the infected colon and closure of the fistula, after signs of infection had subsided. Chronic septic foci developed subsequently in 14 patients of the entire group.

It was emphasized that patients with diverticulitis should be kept on a strict mineral-oil régime with a check-up examination by barium enema at yearly intervals. If complications result, despite this careful medical treatment, surgery such as has been described must be carried out, depending upon the type of complication

Chronic Intractable Ulcerative Colitis

It has been only within the last 10 years that radical surgical measures have been employed to any extent in the cure of chronic ulcerative colitis. We all know that for many years appendicostomy, cecostomy, and ileostomy have been considered curative procedures, but in the light of our present knowledge these are thought to be of little benefit. Previously, the entire diseased large bowel was rarely removed, and only in 1 or 2 instances by any individual surgeon Howard Lilienthal, of New York, in 1899, was one of the first American surgeons deliberately to perform colectomy for what was previously diagnosed a chronic intractable case of this disease in a young woman, 25 years of age. The outcome was successful and the patient is still alive

H W. Cave⁵⁴ points out that failure of medical measures when this disease has reached the intractable stage has led to surgical intervention in an increasing number of cases. No clinician of wide experience with this disease at the present time is willing to accept the term "cure" It is true that not infrequently conservative measures have been followed by temporary improvement, but unfortunately the improvement has not been sustained It is unlikely that after any given period of freedom from activity the disease will not exhibit a recrudescence. Clinicians generally are now admitting that many patients have been lost in the

past because radical surgical measures were denied them.

Indications for Surgery—The indications for surgery can be based fairly accurately on the clinical picture: (1) The effects of toxemia and sepsis; (2) local symptoms referable to the bowel and by the use of roentgenograms; (3) fistulas, sinuses, hemorrhages, and perforations, either subacute or chronic, and strictures; and (4) where there exists a diffuse polyposis with or without malignancy.

During the past 3 years, there was what was considered an unusual opportunity to study intensively many patients suffering from ulcerative colitis A special thoroughly equipped laboratory was established for the sole purpose of investigating this and allied diseases. So far, many of these patients have proved temporarily amenable to medical treatment. Some have become surgical responsibili-One hundred and sixty patients with this disease have been treated in Roosevelt Hospital Twenty-nine have been subjected to surgery, and it is from this experience that certain deductions have been obtained which Cave believes worthy of presentation. The following operations have been performed on 29 patients

Heostomy .	21
Heosigmoidostomy .	3
Partial colectomy with low transverse colos-	
tomy .	2
Partial colectomy with removal of rectum	2
Colectomy	11
Colectomy with removal of the rectum	3

There are 4 types of the disease. (1) Mild cases, at least temporarily arrested and perhaps cured by medical management alone; (2) acute fulminating, frequently fatal; (3) chronic continuous; and (4) chronic with remissions. Confusion exists in the minds of many observers as to when the stage of intract-

ability has been reached, and there has been a diversification of opinion up to the present as to the proper time for surgical intervention. These 2 problems appear often difficult of solution, yet must be faced and solved if successful outcome is to be expected. It is considered necessary that all patients suffering from this disease should be meticulously studied, and some over a prolonged period of time. In the acute fulminating forms prolonged study wastes time, increasing morbidity and mortality. Needless to say, vitamin and other deficiency states should be rectified and all foci of infection eradicated. Considerable reliability can be placed on comprehensive roentgenograms, and particularly on proctoscopic examinations (for 90 per cent originate in the rectum).

The x-rays show characteristic shortening of the entire colon, narrowing of the lumen, mucosal destruction and absence of haustral markings. The normal angulations at the flextures tend to approximate right angles. The barium enema demonstrates a rapidly filling colon with hyperirritability of the involved segments. Such a picture is a clear indication of the removal of the diseased colon

The Selection of Operative Procedure—Cave feels justified in emphatically stating that whatever procedure is chosen, and no matter how many stages are found necessary, all of the diseased bowel should be removed, otherwise a cure cannot be hoped for. Due to the markedly debilitated condition of these individuals, 2, 3 and even 4 stages may make for added safety.

Ileostomy is the first stage in 75 per cent of the cases It is important that the terminal ileum be divided in an area which is not involved, whether it be 6 inches from the ileocecal valve or 3 feet from the ileocecal valve. The ileos-

tomy should be placed on the anterior abdominal wall at a point where it can be cared for easily. The proximal loop should be drawn well out, 3 or 4 inches if possible, and not sutured in any manner to the anterior abdominal wall, for no matter how carefully placed the sutures are through the serosal surface, in coughing or straining after operation, leaks may occur and annoying fistulous openings result. Cave has found that ileostomies placed too close to the midline predispose to intestinal obstruction, on account of loops of small intestine encircling it. Therefore, a McBurney incision is chosen and the mesentery sutured to the lateral peritoneal reflection to prevent loops of small bowel from being caught and becoming obstructed. Cave believes the practice of exploring the abdomen at the time of the performance of ileostomy a pernicious one. It is frequently safer to bring out the distal end as a mucous fistula rather than to turn it in and drop it back, as was originally advocated by Rankin Ileostomy is accompanied by a relatively high mortality, due, the author believes, principally to the fact that these patients are brought to surgery too late. It is an undeniable fact that ileostomy alone has, in a few authentic cases, proved not merely palliative but curative.

Ileosigmoidostomy has been used as a first stage procedure in a small group of individuals where the rectum has been previously determined free of the disease When the left colon and rectum are alone involved and it has been accurately proved that the process has become stationary, transverse colostomy is justified as a first stage procedure. Care should be taken that the colostomy in the transverse colon is placed in a healthy segment of the bowel. Over 90 per cent of the patients in Cave's series, following ileostomy, have shown a tremendous gain in

weight, due to diversion of the fecal stream. Four to 6 months are usually allowed before the second stage of subtotal colectomy is contemplated. Cave states that he and his associates have performed subtotal colectomy 11 times, with 1 death. A most striking feature of this seemingly extensive operation has been the mildness of the postoperative reaction, as well as the fact that all of the wounds have healed per primam.

The second stage of subtotal colectomy was carried out through a long left paramedian incision. There are 2 points during this maneuver which have seemed somewhat difficult (1) Starting the mobilization of the distal terminal ileum, cecum, and ascending; and (2) the division of the splenophrenocolic ligament Careful hemostasis must be effected, and warm moist pads used to protect the exposed coils of intestine, diminishing the chance of rapid fall in blood pressure. It has been made a practice to separate the omentum from the transverse colon for the reason that it simplifies the removal of the colon and preserves the omentum for the purpose of covering raw areas. In mobilizing the right colon, it is well to identify the right ureter, particularly in its lower half, and the third portion of the duodenum higher up, which may be easily injured if care is not taken in thoroughly exposing it. A fall of blood pressure not infrequently follows the division of the middle colic artery, and it is at this stage where Cave and his associates have been forced to immediately resort to trans-As has been stated, the most difficult part of the entire procedure is adequate exposure and division of the splenophrenocolic ligament. When this has been accomplished, the left colon is easily mobilized and there is little difficulty in securely closing the stump of the sigmoid colon with several layers of interrupted silk sutures If the bowel at this level is friable, it is safer to bring this out as a mucous fistula instead of attempting closure. A practice has been made at this second stage of peritonealizing all raw surfaces. It does prolong to some extent the operation but it is felt it also minimizes the chance for the formation of adhesions.

The third stage is carried out by the combined abdominoperineal resection some 4 to 6 months later, when there has usually been an appreciable gain in weight and the patient has been rehabilitated After ileostomy, after subtotal colectomy, and after the third stage of combined abdominoperineal resection of the rectum, transfusion has proved beneficial In the poor risk patient, 4 stages are of necessity employed, the second stage may stop with removal of the right colon and a part of the transverse colon, the third stage consisting of removal of the remainder of the transverse colon, splenic flexure, and descending colon

Complications—The most frequent complication following the operations for the cure of this disease is peritoritis. Perforation of the colon has occurred, even though diversion of the fecal stream has been accomplished with ileostomy. Where the disease is far advanced, strictures and massive hemorrhages occur, even though the fecal current has been sidetracked. He is not an infrequent complication.

Of 29 patients sent to surgery, 5 died, giving an operative mortality of 172 per cent.

Acute Volvulus of the Cecum

Volvulus of the cecum occurs rather infrequently according to G Perazzo, et al.⁵⁵ From a study of the international literature it appears that since

1920 about 60 articles have been published on this subject

With regard to the etiology and pathogenesis of this condition, the authors take the following factors into consideration:

- 1. Predisposing congenital causes of which the most important is a hypermobility of the cecum, or an incomplete rotation of the umbilical loop.
- 2 Among the acquired predisposing causes, hyperkinesia of the cecum has been held responsible for the development of the condition As immediate causes, cecal distention caused by a vegetarian diet, constriction of the ascending colon, and insufficiency of Bauhin's valve have been mentioned. Many other pathogenetic theories have also been advanced
- 3 The immediate causes are usually directly related to an exaggerated peristalsis which might be produced by a sudden contraction of the abdominal muscles, sudden cold, the administration of drastic purgatives or vermifuges, the ingestion of ice-cold drinks, traumatism, violent movements of the body involving the abdominal musculature, violent vomiting, strained defecation, and parturition.

Acute volvulus of the cecum has a stormy and abrupt onset accompanied by vivid pain localized in the right iliac fossa Vomiting appears early. At first bilious, the vomitus soon becomes stercoraceous Defecation does not cease abruptly, the complete abolition often being preceded by diarrhea The patient's facial expression suggests acute illness, the tongue is dry, the pulse is accelerated, and the temperature is usually normal or, at most, slightly raised The abdomen appears symmetrically distended, and there may be a moderate rigidity Palpation usually reveals the presence of an elastic, tender, and relatively fixed mass

In untreated cases death occurs usually on the third day following the appearance of the symptoms, but it may be delayed to the seventh day or later. The diagnosis is difficult and is usually made with the aid of an x-ray film interpreted by an expert roentgenologist. The condition is commonly confused with acute appendicitis and cholecystitis. The treatment is exclusively *surgical*. The operation consists essentially in replacement of the cecum into the right iliac fossa and fixation to the tendon of the psoas minor muscle In some cases this operation may have to be followed by an *intestinal resection* or a *colostomy*.

Tumors of Intestinal Tract

Carcinoids—The histogenesis of gastrointestinal carcinoids is still under discussion The tumors are found most frequently in the jejunum and ileum; those of the ileum show a predilection for adults of the male sex and those of the appendix for the female sex. They may be numerous, and their size varies from that of a pinhead to that of a cherry, they are round or umbilicated, hard, and have a large base of attachment One of their principal characteristics is the presence of argentochromophil granules in the cystoplasm of their cells, analogous to those found in the yellow cells of the intestine. Other cellular inclusions of carcinoids are droplets of neutral fat and birefractive crystals of lipoid, and occasionally granules of glycogen The stroma of the tumors is formed by a connective tissue, moderately rich in cells, which are for the most part fusiform, in addition there are lymphocytes, polymorphous leukocytes, plasma cells, and eventually muscular fiber cells. The blood vessels may be scarce or abundant Carcinoids are found at autopsy or at operation; in the latter case they are found usually in the appendix They very seldom cause intestinal symptoms, grow slowly, and, when left undisturbed, may undergo malignant degeneration; however, they are usually benign and metastases are rare,

as only about 30 cases have been reported.

S. La Manna⁵⁶ describes the case of a woman aged 67 years, in whom about 70 tumors, each the size of a small nut, were found. Thirty-one of these, considered primary, were located near the mesenteric insertion, and infiltrated the 3 layers of the intestine; 28 were observed in the jejunum and ileum, and 3 in the cecum and colon. In some tumors of this group, the tunica propria was little infiltrated and some adenomatous branches issued singly from the bottom of individual crypts of Lieberkuehn, which gave the impression of a multicentric development of the tumor; the newly formed tubules perforated the muscularis mucosa and continued into the tumor above it In other tumors of this group, there was no connection with the intestinal glands, and the tunica propria appeared to be intact. There were 40 metastatic nodules, larger than the primary lesions and located in the mesenteric insertion of the intestine, the epiploic appendices, and the mesenterium The histological morphology of the neoplastic tissue was that of a pure adenocarcinoid in all the nodules, excepting 2 in which was found a microscopic nodule formed of solid cellular cords The outstanding characteristic of the tumoral cells was the presence of very fine argentophil and lipoid granules. The interest of the case lies in the observation of primary nodules in the cecum and ascending colon, in which no form of carcinoid has as yet been reported, and in the decidedly adenomatous structure of the nodules.

Malignant Tumors of the Small Intestine — Malignant tumors of the small intestine may be classified according to their gross characteristics into annular and asymmetrical tumors. The carcinomas are usually annular, while

carcinoma tends toward the expansive type of growth.

The duagnosis of malignancy of the small bowel is not often made before operation or postmortem; the extreme rarity of the condition discourages diagnosis. Rowe and Marshall found reports in the literature of 339 tumors of the small bowel, of which 38 (4.9 per cent) were malignant. Ackman reported 600 cases of intestinal carcinoma in the Montreal General Hospital, of which only 7 were true carcinomas of the small intestine.

D. T. Chamberlin⁵⁷ states that if carcinoma of the ampulla of Vater is included, the duodenum leads as the most common site of carcinoma of the small bowel. The jejunum is next in frequency and the ileum last. The average age of all patients whose cases have been reported in the literature is from 45 to 50 years The symptomatology varies with the size and character of the tumor and its position in the small intestine. The closer it is to the pylorus, the more acute the symptoms are when obstruction sets in. The duration of symptoms may be as short as 2 months or as long as 5 years, depending upon the character and position of the tumor Carcinoma which occurs proximal to the ampulla of Vater produces symptoms that are in no way different from those present in pylorus obstruction due to any other cause Cancer of the ampulla itself produces painless, uninterrupted, obstructive jaundice and dilation of the gall-bladder, and cannot be distinguished clinically from carcinoma of the head of the pancreas Cancer occurring distal to the ampulla in the duodenum and upper jejunum results in slowly progressive obstruction with severe cramp-like epigastric pain, at its peak 2 or 3 hours after meals.

Tumors in the jejuno-ileal region make themselves known by 2 groups of

symptoms. In the first group there are vague symptoms, fairly constant and progressive. Malaise, anorexia, and weight loss are usually present; anemia is a frequent symptom. The pain is shifting, dull, and cramp-like in character. As the lumen of the bowel is encroached upon, vomiting once or twice a week may occur, with partial relief of the symptoms. One type of malignant tumor does obstruct, but grows away from the lumen of the bowel. In such cases the only finding will be a hypochromic anemia, until the mass grows large enough to be palpable

The prognosis of carcinoma of the small bowel is generally poor. The cancer has a tendency toward early metastasis to the mesenteric lymph nodes, peritoneum, liver, lungs, bones, and spinal dura, in the order named X-ray findings often make a diagnosis possible only after metastasis has taken place Kiefer gives the average duration of life after resection as 1 year, and in his report of a series of 11 cases of malignancy of the small bowel there was only 1 patient alive 5 years after a resection for carcinoma of the jejunum.

The treatment is entirely surgical, and the most difficult part of the problem is to recognize the lesion early enough for a hopeful prognosis

During the past 5 years there have been 11 cases of malignant tumor of the small intestine, of which only 4 were diagnosed as such before operation. Six patients were found to have carcinoma, and 3 lymphosarcoma All 9 patients were operated on for obstructive symptoms. The 3 cases of lymphosarcoma were all in younger patients. The earlier appearance of lymphosarcoma is frequently noted in the literature. The lymphosarcomas take a very rapid course so that there is not time for the development of a profound anemia before ob-

structive symptoms supervene. The x-ray examinations of the small intestine are carried out by means of a barium meal on a fasting stomach and films of the abdomen taken at hourly intervals for 6 hours. The author reports 9 cases of malignancy of the small bowel which came to operation in the Lahey Clinic, Boston.

Carcinoma of the Large Intestine —One of the reasons that the end results of radical removal of segments of the colon for carcinoma of that structure are so good (42 per cent of the patients are alive and well without recurrence over 5 years after operation at the Lahey Clinic) is due to the fact that 75 per cent of the malignancies of the large bowel occurred in the descending colon, sigmoid, rectosigmoid and rectum. The good results are related considerably to the fact that lesions as close to the anus as those located in these segments are tend to produce early attention—attracting symptoms so that diagnoses are made in time to obtain good end results

The experience at the Lahey Clinic⁵⁸ in carcinomas of the sigmoid and rectum, where over 1000 patients have been operated upon, shows that in 80 per cent of the cases, with lesions at these levels, were palpable either through the abdomen or by rectum. When one also realizes that the feces at this level are solid and thus tend to produce early obstructive lesions and, in ulcerating lesions, bleeding, it is likewise obvious why these lesions give early evidence of their presence.

In an analysis of the histories in 100 proved cancers of the right colon, 100 proved cancers of the left colon and 100 proved cancers of the rectum it was found that of the entire group, there was an alteration in bowel function or abdominal cramps or pain or abnormal stools in 977 per cent of the cases When

TABLE 5									
Symptoms	OF	CARCINOMA	OF	THE	Colon	AND			
RECTUM (300 CASES)									

	Rec- tum, Per cent	Lett Colon, Per cent	Right Colon, Per cent	Total, Per cent
Blood in stool .	86	46	9	46
Altered bowel function	79	82	81	80
Abdominal cramps or pain None	7 2	77 2	86 3	47 2 3
			·	

(Lahey Am J Surg)

these figures are analyzed, as shown in Table 5, however, it is to be noted that in the rectum 86 per cent had abnormal stools, in the left colon 46 per cent had abnormal stools, but in the right colon but 9 per cent had abnormal stools

In lesions of the right colon, therefore, the feature in the history of abnormality in the stools which is so often present in malignant lesions of the left colon and rectum is lost

It has often been stated that the physiologic function of the right colon plays a considerable part in the symptomatology of lesions in the cecum and ascending colon and likewise has much to do with the mortality of operative procedures in this region

Due to the fact that the contents of the right colon are liquid in character, and that the liquid contents of the right colon are rich in highly virulent organisms, operative procedures such as direct anastomosis when associated with any contamination are particularly apt to result in peritonitis

Likewise, due to the fact that the contents of the right colon are liquid in character, rarely does one see obstructive symptoms in malignancies at this level until the lesions are so well advanced that they completely or almost completely encircle the caliber of the

colon and are thus often in late and inoperable stages. The only exception to the appearance of obstructive symptoms early in lesions of the right colon is when the malignancy of the cecum is close to the ileocecal valve and involves that structure Relatively early and relatively small lesions in this location can produce obstructive symptoms even up to complete obstruction.

The outstanding clinical feature by which early diagnosis may often be made in lesions of the cecum and ascending colon is secondary anemia Why secondary anemias should be so consistently associated with malignancies of the cecum and ascending colon has never been adequately explained. It has been suggested by many that absorption of the noxious toxins from the highly virulent organisms in the warm moist culture media of the liquid feces of the right colon through the ulcerating base of the malignant lesion may well explain this secondary grade of anemia. While this is possible, it hardly seems an adequate explanation of the severe grades of anemia, giving the patient the typical lemonvellow color of intense secondary anemias that occur with these diseases. It has often been possible for Lahey to make the diagnosis of probable caremona of the right colon merely from the color of the patient and from his statement before examination that he has vague pains in the right side of the abdomen. Lahey knows of no malignant lesion where such severe blood changes can appear and produce such changes in the facial appearance of the patient as with secondary anemia associated with lesions of the ascending colon. Certainly it is true that there appears to be no parallel situation in malignancy where such severe grades of secondary anemia can be present with the lesion still readily operable and the patient within a stage where radical removal can result in nonrecurrence. Should such severe grades of secondary anemia be found associated with malignant lesions elsewhere, they would in practically all instances indicate metastases and nonoperability of the lesion. One should bear in mind in dealing with lesions of the proximal colon that this exception as relates to the anemia exists.

It is unfortunate that one does not see in lesions of the cecum and ascending colon bright blood in the stools. Should bleeding occur, it becomes so intimately mixed with the liquid fecal contents of the colon at this level that it is recognized only by studies for occult blood Studies for occult blood, however, will rarely fail to show positive findings in the presence of malignant lesions of the right colon In patients suspected of having malignant lesions of the colon anywhere it will always be wise to make careful studies for occult blood because rarely will malignant lesions of the colon at any level exist in the absence of occult blood in the stools

X-ray findings in malignant lesions of the cecum and ascending colon are particularly apt to be confusing. Due to the fact that the cecum and ascending colon often have long mesenteries and are often redundant, when these structures are filled with barium the defects in the outline of early malignant lesions can be so located on the posterior wall that they are overshadowed by the distended overlying redundant cecum and ascending colon and easily overlooked

It will frequently be necessary to repeat barium enemas in patients suspected of having lesions of the cecum and ascending colon and, in addition to that, it will be necessary at times to send these patients home for a period of 4 to 5 weeks and to have them return for repeat enemas to check with the original film. Exclusive of malignant lesions at

the level of the rectosigmoid, Lahey states that he knows of no place in the whole colon where it is easier, particularly in early lesions, to overlook malignancies. It is unfortunate also that palpation of lesions in the right colon is frequently not positive until they are of considerable size and fairly advanced in character. It is easier, as a rule, to palpate lesions in the cecum and ascending colon than in the hepatic flexure where they are so often located deep under the outflaring arches of the ribs at this level.

One should have in mind always in the presence of an unexplained secondary anemia, particularly in any patient within the cancer age, the possibility of a malignant lesion of the ascending colon with little or no symptomatology associated with it. More than once in Lahey's own experience, failure to pay sufficient attention to an unexplained secondary anemia in the presence of other lesions has caused him to fail to diagnose a lesion of the cecum or ascending colon preoperatively only to find it to his chagrin and surprise during an operative procedure for another condition

Frequently, the only symptoms in patients with malignancies in the cecum and ascending colon are quite vague pain and feelings of bowel discomfort in the right quadrant. It has already been stated that when obstructive symptoms are present in lesions of the cecum and ascending colon one may be quite certain that the lesion is late. There is a quite dependable maxim associated with lesions of the large intestinal tract anywhere There seems little question that the majority of the malignancies of the large intestine in the rectum, sigmoid, left colon and right colon originate in lesions which are primarily benign in character, that is, polyps and adenomas surgeons who have had much experience and who are seriously interested in these

disturbances are convinced of the association between polyps and carcinomas of the large intestine. It is for this reason that one may roughly assume that when a carcinoma of the large bowel at operation or x-ray examination has been found completely encircling the lumen of the bowel, its age is usually between 6 months and a year. This is due to the fact that a lateral wall lesion requires from 6 months to a year to encircle the bowel wall completely.

Since the treatment of malignant lesions of the cecum and ascending colon is universally accepted as surgical, the only discussion necessary is regarding the type of surgery to be applied

Treatment — One may remove the right colon by a variety of procedures. Preliminary anastomoses between the transverse colon and the ileum may be established and at the end of 2 weeks the entire right colon may be removed

The entire right colon may be removed at 1 stage and at this same operation the ileum implanted into the transverse colon

The entire right colon with several inches of the terminal ileum and the hepatic flexure may be removed in 1 block together with its mesentery, the ileum may be approximated to the transverse colon, tacked to the transverse colon by the Mikulicz plan and the ends implanted in the wound. This is the procedure which the Lahey Clinic thinks offers the greatest degree of safety to the patient, particularly as relates to the danger of peritonitis.

W. W. Babcock⁵⁹ states the treatment of carcinoma of the colon is the early and radical removal *en masse* of the affected segment with 7 cm or more of normal appearing bowel on each side of the tumor, together with the associated mesentery, tributary lymphatics and if possible any other involved tissues. The presence of small metastatic nodules in

the liver or of enlarged cancerous glands along the aorta does not, in his opinion, always contraindicate the removal of a resectable primary tumor. By the removal of the original growth the patient is largely relieved of obstructive symptoms, hemorrhage, foul discharge, absorption from the sloughing tumor and invasion of adjacent parts, and usually shows a marked improvement mentally and physically. Often he is able to resume his work for a year or more, and finally dies after a relatively painless decline.

In 252 operations for cancer of the colon, metastases to the liver were found in 33 In 12 the invasion of the liver was far advanced or the primary lesion irremovable A palliative colostomy was done in 6 and a simple exploration in 6 In the remaining 21 patients, the primary growth was resected with 3 deaths (14 per cent mortality). A procto-sigmoidectomy with perineal anus was done in 13, a Mikulicz-Paul stage resection in 6, and a resection with end-to-end anastomosis in 2. Of 19 patients surviving the operation, most have lived over a year, 4 over 2 years, 1 woman now 75 years old is active and comfortable after 416 years

Carcinoma of the large bowel may exist for 2 years or more without metastasis. In Babcock's series, symptoms such as colic, melena, change in bowel habit in the form of diarrhea or constipation, or physical evidence of the growth had existed for from a few months to over 5 years before the patient sought relief by operation

The spread of cancer of the colon is chiefly through the lymphatics and portal circulation Babcock's experience confirms the findings of Miles that the lymphatic drift from cancer of the bowel is upward. Babcock recalls no case of lymphatic invasion caudal to the lesion

in the bowel, nor in his series has he observed gross evidence of involvement of the inguinal lymphatics, even from anorectal growths. Metastasis to the skeleton is much less frequent (5 per cent) than to the lymphatics or liver, but may occur early. Quite striking is the relative, slight tendency toward peritoneal diffusion as contrasted with carcinoma of the ovaries, stomach and other organs. Even with colonic growths of long duration it is usual to find only small peritoneal nodules in a radius of but a few centimeters on the peritoneal leaflets adjacent to the tumor. In contrast is the predominant local invasive tendency of the cancer. It tends to ulcerate early, to invade the submucosa and muscularis to the peritoneum, and later to attach to and invade adjacent structures, as the bladder, small intestine, vagina, uterus, broad ligament, or abdominal wall. Beginning in the transverse colon, Babcock has seen attachment and local invasion of the pancreas and a simultaneous perforation and proliferation in both the stomach and small In such cases if there is no ıntestine clinical evidence of metastasis. Babcock has resected the involved colon with the attached involved uterus or involved portions of vaginal wall, bladder, small intestine, stomach, pancreas, or other removable tissue.

The tendency in many cases for carcinoma of the bowel to remain localized for many months should stimulate the surgeon to undertake a very radical procedure even though excision has been considered impossible at a previous operation, and although a palliative colostomy has been done Formidable adhesions may be found quite benign and infiltrative thickening about ureters and great vessels only inflammatory. The author knows of a few situations of carcinoma in which a previous opinion

of inoperability should so often be discounted. On the other hand, too frequently there is found the rarely mistakable infiltration of cartilaginous hardness, the "frozen" pelvis, or the soft grayish material of a degenerated carcinoma invading parts that are not surgically removable.

The local invasion of the growth has 2 important clinical applications. The base of the ulcer is commonly thin and easily perforated by biopsy, or the necrosis produced by radium, fulguration, or electric desiccation. Babcock has seen the secondary peritonitis and localized abscess following a biopsy block an attempt at radical extirpation of the carcinomatous bowel. The malignant ulcer has such an unmistakable clinical picture with its hard, infiltrating, ragged, raised, and rolled borders and central, depressed, irregular crater that the diagnosis can very positively be made by palpation alone Nearly as reliable is the appearance of the growth as seen through a proctoscope.

The author has never seen a mistake made in diagnosing an ulcerating rectal carcinoma by palpation alone, and therefore considers a biopsy both dangerous and unnecessary in this type. Should biopsy be used, only a portion of raised border above the level of the floor of the ulcer should be removed. With projecting polypoid or adenomatous growths a biopsy is relatively safe and is desirable, as with benign clinical features histologic evidence of malignancy may be found Likewise, except to remove small superficial or polypoid adenomatous growths or to restore temporarily a lumen through an obstructing irremovable fungating cancer, treatment by electrical destructive or other local measures should be strongly condemned. Local treatment not only fails to remove involved lymphatics, but histologic studies show the

fallacy of attempting to destroy the primary carcinoma without the full thickness of the bowel. The treatment may reduce bleeding, delay or temporarily overcome intestinal obstruction and thus give the patient a measure of relief and much hope of cure. As with irradiation, these patients are found after months of dangerous delay drifting to the surgical

static growths, have been infrequent. The intradural injection of 10 mg. of pontocaine mixed with 55 mg. of procaine is favored on account of its prolonged action. As a rule this is immediately followed by 100 to 250 cc. of a 1 per cent epinephrinized procaine solution, injected locally During the operation, if the patient is asthenic, from 1 to 2 pints (500)

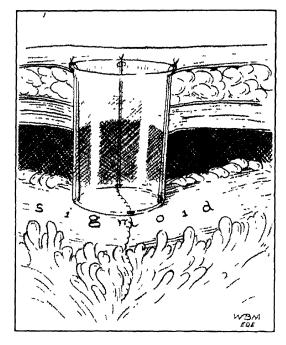


Fig. 23—Glass lump chimney drain, attached by 4 wire sutures over an intestinal anastomosis. The drain is not fastened to the skin

clinic for operative relief. A rather long duration of life may erroneously be ascribed to the treatment

Patients with cancer of the colon who escape a fatal obstruction or perforation not infrequently live 4 or 5 years and some an equally long period after metastasis has developed

Anesthesia—Spinal anesthesia has been used in nearly all Babcock's resections of the colon without mortality or serious complications. Although 37 per cent of the patients were between 60 and 79 years of age, serious postoperative pulmonary complications, except from meta-

to 1000 cc.) of 5 per cent glucose, possibly followed by 10 ounces (300 cc.) of typed citrated blood, is slowly run into a vein. Especially for secondary operations upon patients in very poor physical condition evipal and glucose infusion, combined with local anesthesia, have been very satisfactory to the operator and of great comfort to the patient. A slow intravenous infusion of 5 per cent glucose is started and continued during the operation. As the patient slowly counts, a 2.5 to 5 per cent solution of evipal is injected through the rubber tube close to the intravenous needle, at the rate of

about 15 minims (1 cc) every 10 or When the patient stops 15 seconds counting, the evipal is discontinued instantly, the abdominal incision quickly made and the abdominal wall and subperitoneal layers freely infiltrated with a 1 per cent solution of procame containing 1 minum of epinephrine to each 10 cc. With a pump syringe and a 20- or 22-gauge needle, from 250 to 500 cc of the solution are quickly injected. With this combination little additional evipal may be required and an asthenic patient may doze through an operation lasting an hour and a half from a total of only 06 or 08 Gm. of evipal If the injection is made at the ankle, the body should be tilted head downward, as otherwise a dangerous accumulation of the drug in the lower extremity may occur before an appreciable effect is noted. If indicated, carefully typed citrated blood follows the glucose infusion

It is not uncommon to find the patient in better condition at the end than at the beginning of an extensive operation, and in no case during recent years has sufficient shock occurred under either method of anesthesia to prevent the completion of a radical 1-stage operation

Incision—During recent years for resection of the colon for malignancy or inflammatory disease, Babcock has used oblique lateral incisions of the musclesplitting rectus retracting type almost exclusively. Exception is made if a scar from a previous operation lies adjacent to the operative field. The excision of such a scar better enables the division of postoperative adhesions, the possible correction of an incisional weakness or the avoidance of additional complications in the abdominal wall Fever, leukocytosis, induration of the parietes, tenderness, or fixed mass suggest infection, pericolitis, perforation, or abscess and especially indicate the desirability of a direct approach by an oblique muscle-splitting incision placed over the lesion. Through such an incision infiltrated abdominal wall may be resected, an abscess may be drained, infected bowel delivered and necrotic tissue cared for with the least possible contammation of the general peritoneal cavity,

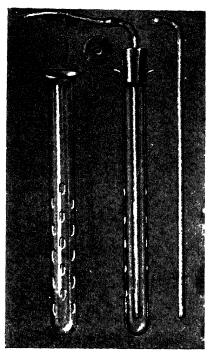


Fig. 24—Sump drain for the continuous evacuation of blood and other fluids that collect in the abdomen after an operation and that might lead to a spreading peritoritis (Babcock Am J Surg)

and with the lowest percentage of hermas from a drained or contaminated wound

These incisions run parallel with the fibers of the external oblique muscle and nerves of the abdominal wall and even after drainage usually leave a fine linear scar. Additional room, if necessary, is obtained by dividing the anterior and, where present, the posterior sheath of the rectus, and by retracting or dividing the rectus muscle. The lateral extension of this type of incision gives good access to the deeply placed ascending or descending colon and facilitates the liberation

and exteriorization of the bowel in a Mikulicz type of resection.

The alloy steel wire sutures with which Babcock began to experiment in 1932 have proved of great advantage for closure of the bowel or abdominal wound.

They do not hold or transmit infection, do not irritate, rarely form fistulous tracts, and therefore do not delay the healing of an infected wound. Either no sigmoid may be reduced by the use of "lamp chimney" and "sump" drains, Babcock feels that the exteriorization stage type of operation is here safer, as it is in any case in which there is pericolitis or abscess.

The "lamp chimney" drains came into use in 1935 in Babcock's attempts to exteriorize and later, after adhesions had formed, to drain the septic gall-bladder.

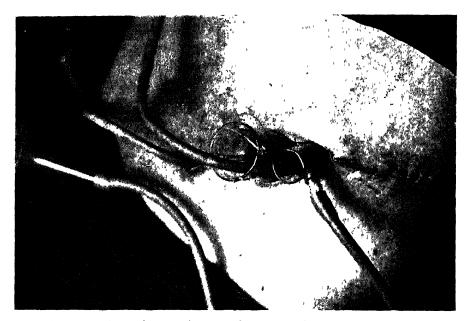


Fig 25—Sump and lamp chimney drains with suction tubes guarding the suture line after a resection and anastomosis of the spleme flexure of the colon. Secondary intestinal leakage occurred in this case but with spontaneous closure of the fecal fistula and recovery. (Babcock, Am. J. Surg.)

anesthetic or only a little local anesthetic is required for the secondary stages of a graded operation, the bowel being without pain fibers

For the right half of the colon a direct anastomosis has in the author's experience given a lower mortality than the Mikulicz type of operation, for both benign conditions and malignant tumors. Conversely for the left half of the colon the Mikulicz operation is considered safer than a 1-stage anastomosis with a functional bowel.

While the mortality from an end-toend anastomosis in the left colon and The device so nearly eliminated the mortality from operating for cholecystitis that the large glass tubes were then anchored over other infected areas and also over insecure intestinal anastomoses (Fig. 23). By adding a soft rubber tube carried to the bottom of the drain, fluid welling into the chimney may continuously be aspirated (Fig. 25). The need for the prompt removal of septic fluids, blood and other culture media, as well as any free peritoneal fluid which may lead to a spreading peritonitis, is especially great after resection of the colon.

From difficulties in obtaining "up hill" drainage, more recently the author had the glass-blower fashion simple glass "sumps" of various sizes and shapes (Fig. 24) These consist of an external collecting glass well or tube which has

machine shop, Babcock has had the miniature motor and pump assembled as a stopper for a wide-mouthed collecting bottle (Fig. 26). This forms a portable single unit for nearly any aspirating service and uses but 1 tube from the

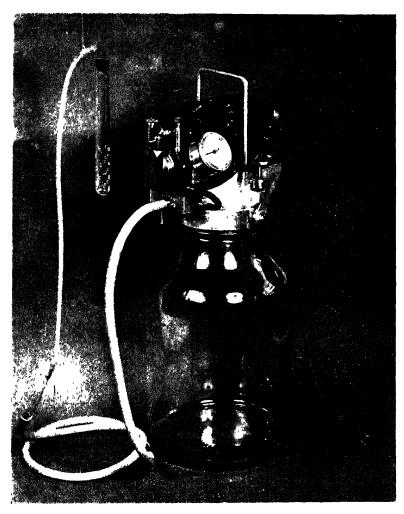


Fig 26—Electric motor with suction pump and collecting bottle attached to glass sump drain for continuous aspiration of an abdominal wound (Babcock Am J. Surg)

multiple perforations so small as to prevent hermation of bowel or omentum of the adult. The internal aspirating tube may be of glass or rubber and is attached to a suction device, preferably a collecting bottle connected with a motor-driven suction pump, although a water spigot aspirator or Wangensteen apparatus may be used. In the hospital

patient When used for an abdominal resection of the colon the suction drainage should be started during the operation and continued during the first 24 or 48 hours or until there is no further collection of fluid. It is especially important to remove blood so promptly that clots do not form and obstruct the tubes. The aspirating tube and any other tubes

(catheter, enterostomy tubes) running from the patient or any pressure port on the aspirator should be marked plainly or so tagged as to avoid dangerous complications from wrong connections. It is obvious that the outer end of the collecting tube must remain open for the free entrance of air.

Babcock's present operative technic is as follows: The diagnosis of low-lying

seen death follow the delayed closure of an ileostomy apparently from this cause alone. During the preparation the general condition of the patient is studied and he is fortified by fluids and a low residue high Caloric diet

Selection of Operation—In removing the cecum and ascending colon usually a 1-stage operation with end-to-end anastomosis is used. This also has given

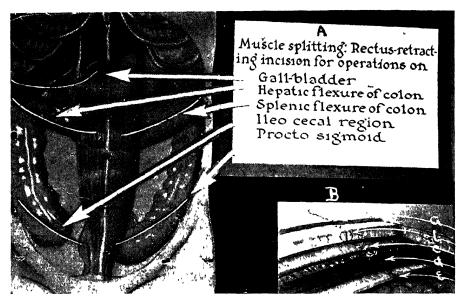


Fig. 27—1, muscle-splitting, rectus retracting incisions used in resection of the colon. B, abdominal wound closure with annealed alloy steel wire. a, continuous sutures of 38 wire for skin, b, interrupted 35 wire sutures for subcutaneous fat, c, d, c, interrupted layer sutures for aponeurosis, muscle and peritoneum. The wire is field in a square knot and the ends cut very short. (Babcock. Am. J. Surg.)

growths is made by the finger and proctoscope, or, for those above the pelvis, by barium enema and roentgen study. Evacuation and decompression of the bowel before operation are obtained by laxatives and repeated irrigations carefully supervised. The author has produced an acute obstruction by a large dose of castor oil

For an unrelieved obstruction a cecostomy or appendicostomy is preferred, as a preliminary ileostomy may lead to inantion from the heavy loss of water and nutriment, not fully compensable by diet, transfusions and infusions. Babcock has

the best results in ileitis. Cutting the ileum obliquely and properly spacing the sutures compensates for a difference in diameter between the ileum and colon.

The inner 1 or 2 rows of sutures may be of continuous chromic catgut or of silk, but for the outer row Babcock prefers the fine alloy steel wire (gauge 35 to 38), the ends being cut very close to the square knot Babcock's experiments show that adhesions form even over very fine (OOOOO) catgut or silk exposed on the surface of the peritoneum, but not over the alloy steel wire As infection or necrosis along the suture

lines frequently occurs, especially after anastomoses of the colon, the author thinks it wise to anchor a tubular glass drain (lamp chimney drain) over the line of union, but not to the skin, with 4 fine alloy wire sutures. This tube is lightly covered with a gauze dressing and through it the united bowel is inspected daily for change of color as well as for offensive odor or high bacterial content of the fluid exudate upon the bowel If the exudate is free from bacterial contamination at the end of 48 hours, the holding sutures are cut and the tube withdrawn. Offensive odor usually is followed by leakage along the suture line and indicates that the tube should be left in place for from 5 to 7 days or until adhesions have firmly walled off the area. In several of Babcock's patients, these tubes have provided an adequate vent for intestinal contents when leakage has occurred and apparently have been life-saving. The fecal fistula which then develops usually closes spontaneously after removal of the glass tube

No other substance with which Babcock's group has experimented, except stainless steel, produces as little irritation in the peritoneal cavity as does glass. Buried in a dog's abdomen, a glass tube remains free from plastic adhesion or exudate at the end of 2 weeks, while a rubber tube is then encased in dense adhesions, and ulceration through the intestinal wall has started. It is to be remembered, that isolating adhesions form very slowly about glass drains, a very desirable feature when prolonged drainage of the general abdominal cavity is necessary.

The tubular glass drain over the sutured bowel may fail to function when leakage occurs on the mesenteric surface or that opposite to the tube. If this is feared a curved suction drain should also be introduced to protect this area. Such a concealed leak may be suspected when the bowel and attached tube become elevated in the wound evidently from pressure from beneath the bowel; or by the pain, tympany, nausea, rising pulse and temperature, and the evidence of free gas and liquid in the abdominal cavity. The treatment is the prompt reopening of the wound and the exteriorization of the bowel ends to prevent further intraabdominal leakage. In many cases a proximal enterostomy also is desirable to relieve the associated inflammatory ileus, and suction (sump drains) should be introduced through the wound, and if there is turbid or odorous fluids, also to dependent portions of the abdominal cavity.

A side-to-side anastomosis is preferred by many operators for ileocolostomy, as it conveniently enables the formation of a large stoma. The end of colon and ileum projecting proximal to the anastomosis should not exceed 5 cm. in length and should be securely inverted and well vascularized, as there is a tendency for the blind ends, especially that of the ileum, to become distended and to leak or cause colic

For several years, Babcock has not used a side-to-side anastomosis Resections in the transverse colon are complicated by the attached gastrocolic omentum and great omentum and by the lack of blood supply when the transverse colic artery is divided. In an obese person particularly, it may be difficult to free the colon from its fatty encasement without interrupting the circulation such a patient a Mikulicz operation may not be very practical even at the flexures and Babcock has observed that along the bulky folds of retained fatty omentum infection may be carried from the open wound into the peritoneal cavity with resulting fatality. As a rule resection

of the transverse colon except at the flexures should be complete. In the obese patient also an end-to-end anastomosis in the transverse colon is particularly subject to necrosis and leakage.

Anastomotic resections of the descending colon and sigmoid have a greater insufficiently radical. The author has modified the technic so that a radical operation may be done and the convalescence shortened, as follows: (1) The cancerous bowel, mesentery and other attached invaded tissues are liberated wide of the growth and exterior-

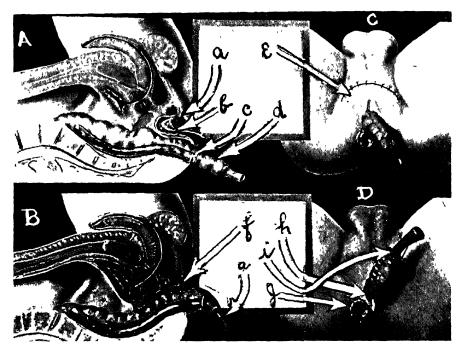


Fig 28—One-stage abdominoperineal proctosigmoidectomy with perineal anus A, the diseased loop of bowel has been liberated from above, then delivered through a median postanal moision and removed B, the perineum, pelvic floor and rectosigmoid have been removed after liberation from below C, for an invading anterior proctosigmoid cancer the pelvic colon and infiltrated portion of the prostate have been delivered through an anterior perineal incision and removed. The sigmoid has been brought through the remaining anus, which has been split anteriorly to relieve tension D, the pelvic colon and sigmoid have been delivered and removed as in A, but the rectum has been amputated just above the sphincers, and the withdrawn sigmoid and in the gutter formed by splitting the anus posteriorly. A glass pelvic drain is in place a, anus; b, recum, c, perforated glass drain; d, sigmoid, e, anterior perineal incision for anterior infiltrating cancers of the rectum, f, defect from excising pelvic floor by a wide elliptical incision, h, posterior split anus; i, rectal tube tired in sigmoid, f, posterior perforated glass tube drain extending along sacral curve. (Babcock: Am J. Surg.)

incidence of infection and leakage than those of the right colon, and therefore a higher mortality unless the fecal current has previously been diverted. As a result and also because the area is beyond the liquid absorbing part of the colon it is here that the Mikulicz-Paul type of operation is especially indicated.

For colonic malignancy the operation has been criticized and discarded as

ized en masse. The wide removal of malignant tissue, an essential part of the operation, is much more important than the peritonealization of denuded surfaces or the formation of a long spur for later division (2) If the arms of the liberated loop of colon can be apposed without tension, they may be sewed together along anti-mesenteric borders. Usually the sutures cause tension and may tear

out or perforate the bowel and Babcock omits them. (3) A narrow sump drain is introduced to be left in for 24 to 48 hours to keep the cavity free from blood and serum. (4) The wound is closed only with layer interrupted alloy steel wire sutures and ligatures to minimize infection. With a protective dressing in place the exteriorized mass is immedi-

by the closure of the wound a short spur has formed. This spur is divided a centimeter at a time, the edges being united with a follow-up suture of interrupted 35 or 36 alloy were in a fine curved needle. By traction on the last 2 sutures introduced, the spur is elevated and stretched, facilitating further incision and the introduction of additional su-

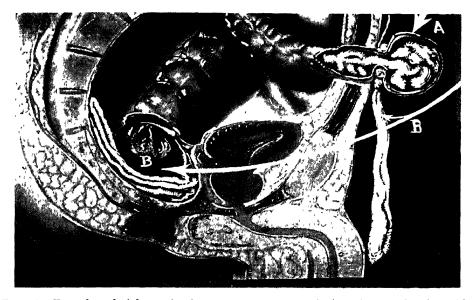


Fig 29—Transfer of abdominal colostomy to perineum A, the colostomy has been liberated and a cap of gauze and rubber has been tied over the end of the bowel with a folded gauze tape B, the liberated bowel and traction tape placed against the floor of the pelvis for withdrawal through the perineum (Babcock Am. J. Surg)

ately cut away between clamps. (5) A right-angled glass tube with well rounded lower border and attached Penrose rubber drain is then tied in each bowel end above the skin level (6) These glass tube vents are removed when leakage from necrosis occurs, usually from the fourth to the sixth day, and wet dressings of a 1 to 500 permanganate of potassium solution are applied and frequently changed to deodorize discharges After 7 to 10 days the necrotic bowel ends are trimmed, and gently liberated from the skin and subcutaneous fascia for suture. Where the arms of the loop of the bowel have been held in apposition

tures Care is taken not to open the peritoneal cavity. Finally, the bowel ends are united as far as is feasible with inverting wire sutures. The skin and fascia are left open, separated and elevated from the sutured bowel by a light gauze packing and the wet permanganate dressing continued

The steps of the Mikulicz operation have thus been modified from such unfortunate experiences of Babcock or his colleagues as death from leaving an obstructive colostomy clamp on the bowel for 2 or more days; ischemic perforation and death from applying a spur clamp over the mesenteric border of the bowel

or from using a devascularized loop; death from pressure perforation due to an indwelling colostomy tube and fatal spreading pyoderma of the abdominal wall from failure adequately to drain the subcutaneous fat after a Mikulicz operation.

In the method just described, as the spur is divided under vision and the edges united by sutures, there is less danger of perforation and leakage and much less necrosis than when the crushing clamp is used. The suture method is nearly painless and relieves the patient of the days of distress and sloughing accompanying the use of the clamp From the short loop used the union obtained is often more of an end-to-end anastomosis than the side-to-side junction of the Mikulicz procedure. Occasionally with the wire sutures, Babcock has had the bowel closed and the patient ambulant by the twelfth day after operation, but usually several steps are required

Colostomy—As nearly all patients object to an abdominal colostomy, Babcock has given much attention to the preservation of a perineal opening. With resection of the colon above the midsigmoid this is not difficult, and with involvement of the lower sigmoid and even the rectosigmoid junction by carefully liberating the pelvic colon to the floor of the pelvis, it is at times possible by traction to deliver the upper rectum through a lower left inguinal incision with sufficient room below the growth to apply a clamp close to the skin and remove the involved segment. An angled glass tube is at once tied in the proximal end of the sigmoid and the cancerous loop with attached mesentery excised Should the cancer involve much of the rectum, or the patient have a thick abdominal wall, an adequate excision by this method may be impossible, in which case the delivery and removal of the liberated rectosigmoid through the perineum is the preferred operation. In a woman of 77 with very friable tissues the rectum below the carcinoma parted. It was cleansed by passing antiseptic gauze through to the anus from above and a large cylindrical glass drain anchored over the open end of the rectum with 4 alloy wire sutures. The proximal rectosigmoid was excised, with formation of a colostomy. An uncomplicated recovery followed.

It is well recognized that resection of the obstructed colon has a high mortality unless the bowel is first decompressed by a colostomy, ileostomy or appendicostomy 2 or more weeks before the major operation The appendix may be used provided it has a sufficient lumen and the obstruction has not reached a critical stage. It is delivered through a short muscle-splitting incision which is closed about the appendix without constricting or dividing the meso-appendix The tip of the appendix is then amputated and a small soft rubber catheter threaded into the cecum, which is gradually decompressed by repeated gentle irrigations, first with warm saline and later with a 5 per cent solution of peroxide of hydrogen. By daily withdrawing the catheter and substituting a well lubricated 1 of larger size. Babcock has been able to insert a 27 F rectal catheter through the appendix at the end of a week

In many middle-aged or elderly patients, however, the appendix is too atrophic to be used and a portion of the distended cecum or lower ileum is withdrawn through the muscle-splitting incision, a segment isolated and emptied with the aid of a non-traumatizing, curved rubber-covered clamp. Two concentric purse-string sutures of fine silk are then introduced in the wall of the bowel, within which, under the protection

of surrounding pads, a puncture is made, and a 14 F. soft rubber catheter introduced and tied in. In closing the wound about the catheter it is best to use only alloy steel wire sutures and ligatures. The ends of the outer purse-string suture are brought outside the wound and tied

ter will usually be found adequate for the decompression of the obstructed bowel.

If the free peritoneal fluid is turbid or shows evidence of bacterial contamination, a long narrow sump drain should be introduced through the wound to the bottom of the pelvis and suction evacua-





Fig. 30—Cancer of the rectosigmoid and attached double-barrelled colostomy of the sigmoid withdrawn in 1 stage through a postanal incision after closing the abdominal wound. I, cancer B, colostomy openings covered with gauze and rubber dam C, traction tape fastened to B. The bowel was adherent and 2 previous attempts at removal through the abdomen had been abandoned. The patient strongly objected to the abdominal colostomy (Babcock. Am. J. Surgery.)

from colostomy 11 years after Miles operation for carcinoma of the rectosigmoid The redundant bowel and scar were excised, the hernia repaired, and perineal anus formed (Babcock Am J Surg)

Fig 31 — Hernia and intestinal prolapse

around the catheter, after having also been used to anchor the bowel to the overlying edge of peritoneum. Under repeated and prolonged irrigation after the patient has been placed in a comfortable position in bed, the small cathe-

tion continued as long as liquid comes away

This simple enterostomy with a small catheter having several openings is preferred because the introduction of a mushroom catheter is more difficult, necessitates a larger opening, and there is risk of greater contamination in the wound. From a large and therefore stiffer rubber catheter, the author has

seen fatal perforation of the bowel due to pressure of the tip of the catheter. In his experience the mortality of a formal colostomy with exteriorized loop for ileus from cancer of the colon is about 15 per cent or over. Where there has been a heavy impaction of solid feces above the obstructing carcinoma while a simple enterostomy and persistent irrigation will relieve the acute and dangerous symptoms, flushing from any single opening may be inadequate to liquefy and evacuate the nearly solid mass Even with a through and through flushing alternately, discharging first from the rectum and then the proximal enterostomy, hours of effort perhaps repeated over several days and the use of many gallons of water may be required before the colon is emptied

As for the abdominoperine il proctosigmoidectomy which is the preferred procedure for cancer of the lower sigmoid and pelvic colon, Babcock believes that a single stage operation with perineal anus may be as radical, more aseptic, rather easier of execution and better for the patient than the conventional multiple or single stage procedures with the formation of a permanent abdominal colostomy In general, surgical opinion contends that an operation without colostomy is less radical. However, in the operation used by Babcock and his colleagues, the ligations are placed as high, the section of bowel, mesentery and peritoneum removed is as great, and an associated panhysterectomy, or resection of the vagina, vesicles, prostate or pelvic floor is as feasible as with any other operation. Moreover, that the colostomy may not have been essential for a radical excision at the original operation is indicated by Babcock's ability to transfer such an opening from the abdominal wall to the perineum at a later time.

The single stage operation with perineal outlet is done without crushing. dividing or opening the bowel until after the wounds have been sutured and dressings in place and, therefore, should be more aseptic than one performed with an abdominal colostomy. In either case in the liberation of the cancer an inadvertent opening of friable bowel or an invasion of a septic focus may occur. That the patient prefers the perineal opening even without sphincter control is the testimony of those Babcock has operated upon, as well as those who have had an abdominal colostomy transferred to the permeum. From about 110 such operations Babcock has learned that a perineal sigmoidostomy has a convenience, an infrequent soiling and discharge of gas, and an expulsive power from the abdominal muscles unequaled by an abdominal colostomy. With regulated emptying of the colon, over onehalf of the patients with the perineal opening can dispense with a protective pad and 85 per cent have infrequent With a few modifications the technic Babcock now uses follows the plan he described in 1932

Elimination of the Abdominal Colos-An abdominal colostomy was transplanted to the permeum in 7 patients. In 4 the colostomy had been a part of an abdominopermeal proctosigmoidectomy for cancer, in 1 patient 11 years, in another 4 years before. In the third patient the cancer had perforated the vagina and invaded the uterus and Babcock had combined a panhysterectomy and resection of much of the vagina with an abdominoperineal proctosigmoidectomy and colostomy, 7 months before. The fourth patient had an en masse resection of uterus, appendages, upper vagina, rectosigmoid and 4 or 5 cm of 1 ureter 11 months before the transplantation The fifth patient had

vertical, very adherent abdominal scars from 2 previous attempts to remove a cancerous rectosigmoid. On account of adhesions the growth had been considered irremovable and a double-barrelled sigmoid colostomy was done. Without disconnecting the openings in the sigmoid, adhesions were divided and the rectosigmoid and colostomy liberated from above and then delivered through the perineum with the formation of a perineal anus (Fig. 30). All 5 patients had satisfactory recoveries

The advantages of the permeal opening were very evident, such as ability to go without a pad or other protection, evacuations occurring every 2 to 4 days instead of several times daily, convenience for irrigation, diminished flatus, and more effective expulsive action of the abdominal muscles The remaining 2 patients were cachectic men One, aged 60, had been treated for over a year by injections A sigmoid colostomy for an obstructing anorectal carcinoma was done 24 days before an abdominoperineal resection with transplantation of the colostomy to the permeum Despite preoperative evacuant measures the colon contained much impacted fecal material The advanced adherent carcinoma ruptured in delivery. The patient died of a postoperative peritonitis. The seventh patient, aged 70, had a rectosigmoid carcmoma On account of his great debility, a 2-stage operation was tried, a doublebarrelled sigmoid colostomy being done at the first stage, and a proctosigmoidectomy with delivery of the bowel and of the colostomy through the permeum at the second stage 15 days later. The patient died later from a necrotic metastatic carcinoma of the lung.

These experiences have confirmed Babcock's impression that it is easier and safer to do a proctosigmoidectomy in 1 instead of several stages, that any

preliminary colostomy should not be in the field of the radical operation, and that while a permanent palliative colostomy for cancer of the rectosigmoid may properly be placed in the sigmoid, a temporary colostomy for intestinal obstruction should be in the cecum or proximal colon. It also was evident that it is safer to reoperate in the field of an old rather than a recent colostomy With chronic obstruction in the terminal bowel a bulky fecal impaction may extend back to the cecum and be very difficult to remove by retrograde irrigation through a sigmoidostomy. In transferring a colostomy to the perineum, if there is a double-barrelled opening, it is usually better to isolate and ligate the ends of the bowel as 1, covering the openings with a single protection of gauze and rubber drain, securely ligated in place rather than to divide the bowel.

Technic of Transferring an Abdominal Colostomy to the Perineum—The colostomy opening is plugged with antiseptic gauze and closed with sutures, and when liberated, the end of the bowel is covered by a cap of gauze and rubber dam securely tied on with a long tape (Fig. 29). The sigmoid segment and, if necessary, the descending colon are then sufficiently mobilized from peritoneal and other attachments to slide at least 12 cm (5 inches) below the posterior pelvic The soft tissues in the midline close to the sacrum are divided and then tunneled to the pelvic floor until a channel is formed through which the sigmoid may easily be drawn. The tape is packed in this tunnel, the end of sigmoid laid over the opening and abdominal wound With care not to injure the urethra or bladder the perineal scar is opened from below and the tape and attached sigmoid pulled through A glass tube drain is introduced at the side of the coccyx or through the incision back

of the sigmoid. A rectal tube is fastened in the sigmoid to prevent soiling during the first few days after the operation. The glass drain is usually removed in from 24 to 48 hours.

Operability and Mortality-Unfortunately, universal standards have not been adopted as to the operability of persons having cancer of the large intestine. Babcock has attempted a radical operation in any case in which it offered a chance of prolonging the patient's life or rendering it more comfortable even though it could not be curative. Thus of about 265 patients seen during more recent years, operation was done in 252, which included removal of the cancerous segment in 212, an operability rate of 84 per cent, if the patients not curable but relievable are included. In about 40 per cent of the patients symptoms indicative of cancer had been present over 1 year and in 21 per cent from 2 to even 5 years before the operation. At the time of operation 37 per cent of the patients were over 60 years of age, and 11 per cent between 70 and 79 years. As has been indicated, metastases were not uncommon in those considered to be radically operable With such an extremely distressing and fatal disease as cancer the patient has little to lose, except pain, if given the benefit of every surgical doubt

An enlarged lymph node in the field of the cancer is frequently found free from malignancy in the laboratory. Occasionally ominous physical signs, as fixation, the intense anemia of a cecal cancer, or a report from previous operation that the growth was adherent and irremovable, will be found due to a benign cause or to a malignancy that can be extirpated

Mortality and Babcock's concepts of operability are closely related. Of the 252 patients 46, or 18 per cent, died after operation while in the hospital. The high-

est mortality occurred in cases with perforation and resulting peritonitis, abscess or fistula; 15 cases with 9 deaths (60 per cent). Next was the mortality from direct anastomosis, 9 deaths in 26 cases, almost entirely from resections of the functional left colon. While the mortality has been reduced by the recent use of better drainage, and while the operation is believed to be safer than a Mikulicz resection for the right colon, it has now been largely abandoned for the left side of the colon unless the fecal current has previously been diverted

Colostomy—an operation under other circumstances of very low mortalityhad a mortality of 30 per cent in the 23 advanced cases in which it was used as a palliative measure The operation renders these patients disgusting to themselves and to their friends, who do not care to take them from the hospital and often leave them until they succumb to the progress of the disease Babcock's present tendency is to do very few socalled palliative colostomies. In the face of obstruction he depends upon a low residue diet, irrigations, and duodenal suction. For the patient whose advanced disease leaves him but few remaining days. Babcock thinks it better to let him die obstructed than to inflict the nuisance of a colostomy upon him and his attendants

The operative mortality is much reduced if we eliminate those shown by autopsy to have been hopelessly diseased by metastasis or those it was learned by experience were inadequately drained at the time of operation. Then the mortality in Babcock's series from abdominoperineal proctosigmoidectomy with perineal anus drops from 20 per cent to under 6 per cent, from perineal proctectomy from 11 to under 4 per cent, and from the Mikulicz-Paul operation, from 15 per cent to about 5 per cent

PANCREAS

Acute Pancreatitis

Acute pancreatitis has been described as being one of the most dramatic of all diseases. It has been placed in the same category as ruptured ectopic pregnancy, since, in both, the classical description is one of profound shock. This impression in the latter instance has been changing because now most patients with ectopic pregnancy are operated upon before the lesion ruptures In pancreatitis, however, many physicians are still reluctant to make the diagnosis in the absence of shock and cyanosis An analysis of the cases presented by L S. Fallis and G Plain⁶⁰ demonstrates that such findings are quite unusual. It was the relative mildness of symptoms and findings in severe cases in contrast to the classical description that aroused interest and prompted a study of the authors' case records They have noted that increased interest in the subject has brought about improved results in both the diagnosis and treatment of their own cases, for example, the 3 cases seen after this work was started were correctly diagnosed preoperatively.

The study covers 26 patients with acute pancreatitis operated upon at the Henry Ford Hospital. Cases not coming to operation and those definitely secondary to a perforating peptic ulcer are not included.

Most patients with acute pancreatitis present clinical features which lead the observer to suspect disease of the biliary tract. On admission to hospital the first examiner recorded his early impression of the condition. Cholecystitis and chole-lithiasis headed the list of possibilities in 16 of the 26 cases, or 61.5 per cent of the total. Perforated ulcer was considered on 7 occasions and acute intestinal obstruction in 4 instances. Acute

appendicitis and acute diverticulitis were both mentioned twice, while tabetic crisis, angina pectoris, general peritonitis, subphrenic abscess, ureteral calculus, and mesenteric cyst each entered the diagnostic field once Acute pancreatitis was mentioned as a possibility 10 times.

A definite diagnosis of acute pancreatitis was made in 8 cases, or 308 per cent of the cases. In 1 patient the diagnosis was easy because he had been operated upon before for the same condition. The diagnosis in 3 patients was based on the presence of a bluish discoloration around the umbilicus, the socalled Cullen's sign In the authors' experience the presence of an upper abdominal mass and a positive Cullen's sign as was found in 2 of the authors' cases provides the only definite diagnostic criteria, for, of the 8 positive diagnoses, only 2 were made without 1 or the other of these clues.

The finding of 73.1 per cent of the authors' patients with pathologic gallbladders serves to emphasize the relationship which has been stressed by all authors on the subject. The gall-bladder and pancreas have much in common, their ducts normally enter into the duodenum together, though the exact relationship varies, their blood supply arises from the same source, and their lymphatic vessels have a rich anastomosis Of the 3 possible routes for spread of infection from the gall-bladder to the pancreas, the lymphatic route appears to be the most feasible. Some support of this theory is given by a consideration of the frequency with which mild degrees of chronic pancreatitis are found in cases of cholecystitis and cholangitis

Biliary calculi were present in the gall-bladder in 15, or 80 per cent, of the 19 cases in which the gall-bladder was obviously diseased, but were found only

twice in the common duct at operation. However, in 1 patient who expired, autopsy revealed a single small stone plugging the ampulla of Vater. No doubt there were other examples of common duct calculi in the series, for, even under the most favorable conditions, small stones are frequently unrecognized and all the more so when exploration must be hurried because of the condition of the patient Gall-stones, of course, can be a factor in acute pancreatitis only under circumstances in which obturation of the ampulla of Vater permits reflux of bile into the pancreatic ducts. The anatomic variation making this possible probably occurs in about 60 per cent of cases, as shown by reports fluctuating from 3 5 per cent to 89 per cent.

The question which naturally arises is, why is pancreatitis so infrequent if it is caused by spread of infection from the gall-bladder either through the lymphatics or by way of the biliary passages? There were 1716 cholecystectomies performed at the Henry Ford Hospital during the same period the 26 cases of acute pancreatitis of this series were observed. This gives a ratio of 66 to 1, a figure almost identical with that given by Abel, who found 30 operations for acute pancreatitis and about 2000 operations in the biliary tract. Furthermore, if the gallbladder origin hypothesis is the correct one, acute pancreatitis should be more commonly associated with acute than with chronic cholecystitis and yet the authors show the reverse to be true, for the gall-bladder was acutely inflamed in only 154 per cent of the cases. Finally, how are we to explain these cases of acute pancreatitis in which the gall-bladder shows no evidence of disease? The clinical course of the disease in fulminating cases suggests an overwhelming infection. It may be that a generalized infection becomes localized in the pancreas in the same manner that the lungs bear the brunt of a pneumonic infection.

Treatment — The best results were obtained in those cases where the operation simply consisted of drainage of the lesser peritoneal cavity. Eleven patients were treated in this manner with 5 deaths, a mortality rate of 27.7 per cent. When cholecystostomy was added, as it was in 13 cases, there were 8 deaths. a mortality rate of 61.8 per cent: and death occurred in 2 of the 4 patients in whom the gall-bladder was removed and the common bile-duct drained, a mortality of 50 per cent The finding of a mortality rate of 46 1 per cent, even in such a serious disease as acute pancreatitis, suggests that the method of treatment currently in vogue should be reviewed critically. It has been the procedure in the authors' clinic to operate upon all cases of acute pancreatitis as soon as they are diagnosed or suspected The fluid balance, of course, is restored and blood transfusions are given to forestall or combat shock. All the patients in the series except the last 3 were treated in this manner

It is interesting to conjecture why early authors on the subject felt that it was so necessary to evacuate the products of pancreatic necrosis Their teaching has been followed by most surgeons in spite of the work of Whipple, who, as long ago as 1913, demonstrated that the peritoneal exudate in acute hemorrhagic pancreatitis was innocuous when injected into the veins and peritoneal cavities of animals. The modern trend is to treat acute pancreatitis conservatively and to operate only when a definite mass appears. The results of drainage of these pseudocysts and abscesses are extremely good and the mortality is low

The proponents of the conservative treatment feel that immediate operation does not benefit the fulminating cases

and that the added insult of the anesthetic and the operative trauma may turn the tide against the patient. Their contention receives further support from the conclusions of practically all observers that the outcome of a case depends on the degree of involvement of the pancreas and that this is often determined by the time the patient is seen by the surgeon. Decompression of the biliary system, in the authors' cases, did not fulfill the theoretic expectations since the mortality rate in those cases in which cholecystostomy was performed was almost double that of simple drainage of the lesser peritoneal cavity. However, it is conceivable that in the early edematous stage of acute pancreatitis decompression of the biliary system might be of value because there are cases on record in which only edema of the pancreas was found at operation, and yet the patient went on to die of a fulminating pancreatitis. The great drawback of the expectant attitude is in the difficulty of making an accurate preoperative diagnosis Directly as a result of this study the authors have treated conservatively their recent cases of acute pancreatitis, including the last 3 of this series. All of the patients recovered following drainage of abscesses or pseudocysts.

The high mortality of acute hemorrhagic pancreatitis has induced many authors to investigate the cause of this condition. A. Pavlovsky⁶¹ thinks that today there is a tendency to use the same treatment for the many different types of acute pancreatitis. Some authors consider operation the treatment of choice, while others do not favor operation; a certain amount of confusion exists on this point.

Pancreatitis may be classified as follows: (1) Classic, acute hemorrhagic pancreatitis. (2) acute edema of the pancreas with all of its variations, and

- (3) serous hemorrhagic apoplexy of the pancreas.
- 1. The clinical symptoms of acute hemorrhagic pancreatitis are classic. Operation shows cytosteatonecrosis of the gland, the peritoneum, and the omentum. In addition, there is a hematoma or hemorrhage and often acute distention of the biliary ducts associated with a gall-bladder filled with stones.

Pavlovsky believes that the condition in all cases in this group can be improved by operation and that in none will it show improvement following non-operative measures. Surgery consists chiefly of relief of the tension of the biliary tract by means of cholecystostomy and drainage of the necrotic focus in the pancreas. The author concludes that only operative measures can give any hope of success, even if the rate of mortality is very high.

2 Acute edema of the pancreas has received the attention of many authors in recent years. The author believes that, as the condition does not always precede acute hemorrhagic pancreatitis, the treatment may be non-operative and should be as energetic as possible. In this way, emergency operations with all their dangers can be avoided If we study the clinical records of many patients with acute biliary colic, we very often find that during the attacks there is abdominal pain with irradiation to the back, as well as a certain degree of peripheric shock These symptoms show the involvement of the pancreas and indicate the urgency of an operation designed to correct the biliary disease

Medical treatment consists of the injection of hypertonic saline or hypertonic glucose solution, the administration of cardiac tonics, adrenalin or epetonine, caffeine, or camphor derivatives, and, in serious cases, blood transfusions.

Recovery is very slow, often requiring 2 or 3 days, but the best procedure is to wait and operate later, when the patient is in better condition.

The author states that early operation in acute edematous pancreatitis has given poor results, as the mortality is around 50 per cent. Some authors believe that operation should be avoided in every case, as the distinction between edematous and hemorrhagic pancreatitis is quite difficult. The statistical results are very different, the mortality ranging from 0 to 22 per cent

The distinction between the 2 kinds of pancreatitis can be made through observation of the symptoms, especially at an early stage of the condition, if energetic clinical treatment gives no success, the hemorrhagic form is sug-The alarming symptoms of gested edematous pancreatitis, very often complicated by hepatic colic, respond slowly to medical treatment. On the other hand, the persistence of a serious condition indicates the possibility of a hemorrhagic pancreatitis. Chemical examinations give modifications of the normal values in both forms.

3 Serous hemorrhagic apoplexy of the pancreas. According to the new concepts of Gregoire, Silvestri, and others, acute pancreatitis is the result of a general disturbance with special emphasis on the pancreas, depending on local conditions. Hemorrhagic congestion is produced through excitation of the splanchnic nerve. Visceral hemorrhage is the consequence of a circulatory change, produced by disturbances of the neurovegetative system. The lesion may be chemical or physical; the important thing is the involvement of the vasomotor centers.

Many cases in which the classical picture of acute hemorrhagic pancreatitis was the cause of death did not reveal

any lesion of the biliary tract. The only explanation which could be given was the existence of neurovegetative lesions. Sometimes the difficulty was in the liver; if the hepatic cells failed in their function, the liver could not prevent severe shock, and the pancreas was the site of a congestive hemorrhage, caused by the suppression of essential functions of the liver.

The symptoms are extreme epigastric pain, peripheric collapse, descent of the blood pressure, and, in contradistinction to hemorrhagic pancreatis, a very marked resistance of the abdominal wall.

Operation shows an infiltrating edema of varied extension, including the gland and the depending omentum. Stains of cytosteatonecrosis are exceptional. The biliary tract seldom presents lesions.

Treatment must be very energetic. **Adrenalin** must be given to combat shock and hepatic insufficiency must be overcome

Gregoire and Couvelaire think that operation must be performed for the following reasons. Diagnosis is never certain; medical treatment very seldom gives relief from pain, and the pancreas must be explored because of the possibility of a necrotic focus which may need a special type of drainage.

Pancreatic Fistula

The effect of ephedrine on pancreatic secretion and its use in the management of patients having a pancreatic fistula is described by C B Craft 62. The results of animal experimentation clearly indicate that ½ grain (10 mg.) of ephedrine given subcutaneously decreases the volume output of pancreatic secretion. Like epinephrine, ephedrine probably produces its inhibitory effect on the secretion of pancreatic juice through its vasoconstrictor action on the blood vessels of the pancreas, which results in a

decrease in the minute flow of blood to the pancreas and a decrease in secretion of pancreatic juice. Ephedrine begins to exert its vasoconstrictor action about 10 to 15 minutes after injection and continues to exert its effect for the next 20 or 30 minutes

In the doses used to decrease the secretion of the pancreas, ephedrine produced no toxic manifestations in animals Ephedrine is a drug which should be tried for the reduction of pancreatic secretion in cases of pancreatic fistula. The amount of ephedrine that would be required to reduce the secretion of the pancreas in man cannot be stated; however, a single dose of 6 grains (389 mg.) or the administration of $2\frac{1}{2}$ grains (160 mg.) every 3 or 4 hours during the day and night has produced no serious results.

Silica gel has proved to be very valuable in the control of the skin excoriation and tissue digestion in 2 clinical cases. It has been used on the theory that it absorbs enzymes. It is a neutral powder, very soothing, non-irritating, and easily applied.

Glandular Cysts of the Pancreas

A complete survey of the literature and the presentation of 19 cases of glandular cyst of the pancreas is presented by L. Massé, *et al* ⁶³. The 19 cases include only those in which the glandular nature of the cyst was recognized both at operation and on histological examination.

The authors make the following histo-logical classification of glandular cysts of the pancreas (1) Polycystic disease of the pancreas, (2) cystic lymphangiomas, (3) dermoid cysts, (4) canalicular cysts, (5) cystic adenomas, and (6) cysto-epitheliomas. Under this classification the 19 cases presented 1 polycystic tumor, 2 canalicular cysts, 10 cystic

adenomas; 2 adenocarcinomas; and 4 vegetative tumors of the cystoepithelioma type

From the histological and pathological studies, 2 types of cysts are recognized: (1) Those which have developed in the pancreas itself, and (2) those which have developed at the expense of embryonic débris included in the pancreatic parenchyma in the course of development. These are the vegetative cysts which behave almost as malignant tumors. Simple marsupialization will cure the first type, but only total excision will cure the vegetative cysts.

The macroscopical appearance of the cysts is as follows Most of the cysts have a smooth external wall with a slightly bluish or sometimes yellowishwhite appearance The wall may be covered with very large dilated veins, is usually thickened to at least 2 cm, and is resistant. The interior of the cyst is variable according to the histological nature, it is sometimes unilocular, sometimes multilocular, and sometimes contains budding vegetations The liquid contained in the cavity may be definitely bloody, chocolate colored, or clear, viscous, and opalescent. The dimensions of the cysts are exceedingly variable The pancreatic ferments may all be present or any 1 or any combination may exist

The tail of the pancreas is the most frequent site of origin. The complete removal of these tumors presents serious difficulties, for in developing the tumor contacts or adheres to neighboring tissues such as the duodenal arch, the spleen, the splenic pedicle, or the duodenojejunal angle.

The most frequent position of the cysts is inter-gastrocolic. The tumor compresses the stomach toward the diaphragm and the colon toward the pelvis, and bulges beneath the gastrocolic liga-

ment. Cystic tumor of the pancreas is essentially a disease of adults; 3 patients were under 20 years of age, 3 were between 20 and 30 years, 6 were between 30 and 40, and 7 were more than 40 years of age. The extreme ages were 12 and 62 years, respectively. As to sex, 15 were females and 4 were males

There is no definite symptomatology or pathognomonic manifestation which will permit diagnosis of a cyst of the pancreas In 8 of the 19 cases the tumors were the first symptom, in 5 functional troubles preceded the tumor, and in 6 the tumor and functional difficulties appeared simultaneously Digestive troubles are frequent A pancreatic syndrome of the external secretions has not been noted, nor is there glycosuria. Emaciation was noted in 5 cases In 7 cases the tumor was located in the epigastric region, in 6 it was definitely located in the left hypochondrium, and in 3 it was to the right of the umbilious In 12 cases the tumor was mobile, and in 3 immobile

Roentgenological examination through the use of a barium enema or barium in the gastro-intestinal tract may help in the diagnosis by showing the organs markedly displaced. Urography is of value, as an exact preoperative diagnosis has been made in several instances by this means. Rupture into the peritoneum and jaundice are rare

As regards treatment, these tumors should be excised because they are almost insensible to roentgen rays. Two methods of treatment may be used—marsupialization of simple cysts of the pancreas without vegetation, and excision either of the cyst alone or of the cyst including part of the pancreas. In tumors with intracystic vegetations, only complete extirpation will give a cure, although a cure is not always technically possible. Only tumors limited to the tail

justify *pancreatectomy* and then only if they are sufficiently free

The operations in these 19 cases were: 2 pancreatectomies (left) with 1 death; 2 enucleations; 5 complete extirpations; 1 large but incomplete extirpation, and 9 marsupializations with 1 death.

Carcinoma of Pancreas

Carcinoma of the pancreas is not a common form of malignant disease. It constitutes only from 1 to 2 per cent of all carcinomas. In the management of this disease, difficult problems of diagnosis and treatment are encountered.

This analysis includes 47 cases of carcinoma of the pancreas in which operation was performed at the Lahey Clinic in Boston, 64 with a follow-up note on all patients until the time of death. In 35 cases the diagnosis was made from a satisfactory operative description of the gross pathological change as observed by an experienced surgeon. Seven of the remaining cases were proved to be carcinoma of the pancreas at biopsy, and 5 at autopsy.

The average age of these patients was 50 years, the ages ranging from 31 to 80 years. There were 23 men and 24 women, a higher incidence of women than is usually found in most reports.

The average duration of the disease before admission to the clinic was 3% months, this period ranging from 1 to 9 months. Pain frequently preceded the onset of jaundice. In the order of their frequency, the commonest symptoms of carcinoma of the pancreas were weight loss, anorexia, pain, jaundice, nausea and voniting. Loss of weight was present in 85.1 per cent of the cases. There were practically no disturbances of the bowel function.

On physical examination, abdominal tenderness was elicited in 361 per cent of the patients; it occurred in the epigas-

trium in 5, and in the right upper quadrant in 12. There was no relationship between tenderness in the right upper quadrant and the presence of distention of the gall-bladder. An abdominal mass was palpable in 553 per cent of the cases; it was found in the right upper quadrant in 18, in the epigastrium in 5, and in the right upper quadrant and epigastrium in 3.

The roentgenographic findings of extrinsic pressure on the stomach or duodenum, duodenal stasis, or widening of the duodenal loop are valuable diagnostic data Roentgenograms were taken in 21 cases, 6 were negative, 7 showed extrinsic pressure or stasis with no widening of the duodenal loop, and 8 showed widening of the duodenal loop without extrinsic pressure or stasis. Therefore, positive roentgenological findings were noted in 714 per cent of the cases in which gastrointestinal roentgenograms were taken Such a valuable diagnostic aid should be used more frequently when carcinoma of the pancreas is suspected.

When the common bile-duct is involved, additional diagnostic evidence may be obtained by examination and demonstration of the absence of bile or the presence of blood in the duodenal drainage. Duodenal drainage was done in only 7 cases, but in all of these cases bile was notably absent, and in 2 cases blood was obtained. It must be remembered that carcinoma primary in the bileducts may give similar findings.

Upon operation there was distention of the gall-bladder in 639 per cent of the cases. Metastasis occurred locally or to the liver in 31.9 per cent. The primary growth involved the head of the pancreas in 38 cases, the body in 2, the tail in 1, the entire gland in 4, and the stomach, pancreas, and transverse mesocolon in 2.

The pain associated with this lesion is, however, much less severe and per-

sistent than that associated with gallstone colic. Less than two-thirds of the cases showed jaundice and distention of the gall-bladder. When these 2 factors are present, they are important diagnostic aids, indicating obstruction of the common bile-duct, but they may never occur or may appear as late manifestations of the disease. Anorexia, progressive weight loss, and a dull pain in the epigastrium or right upper quadrant of the abdomen, boring through to the back under the angle of the right scapula, are more suggestive symptoms of this disease. Pain is not entirely due to the distention of the gall-bladder, since there is no definite relationship between these 2 factors. Weight loss was a frequent symptom definitely associated with anorexia and probably caused by a disturbance of the pancreatic function.

Treatment — Many surgical procedures were used in the management of these cases. Abdominal exploration; cholecystogastrostomy, cholecystogastrostomy and posterior gastroenterostomy, cholecystoduodenostomy, cholecystojejunostomy, cholecystojejunostomy, choledochostomy, choledochostomy, choledochostomy, and cholecystostomy and cholecystostomy, and cholecystostomy and posterior gastroenterostomy.

The average length of life of the 38 patients who survived operation, without regard to the method of management, was $8\%_{10}$ months

The pancreas is quite sensitive to radiation. It is distinctly worth while to employ irradiation in these cases after operation as evidenced by the prolongation of life in those in which irradiation was given as compared with those in which irradiation was not used.

The authors have employed 3 types of palliative operation in patients with malignancy of the head of the pancreas

Anastomosis of the gall-bladder to the stomach (cholecystogastrostomy); anastomosis of the gall-bladder to the duodenum (cholecystoduodenostomy), and anastomosis of the gall-bladder to the jejunum (cholecystojejunostomy). Of these procedures, only the last one has now been employed for some years.

Cholecystogastrostomy is an undesirable surgical procedure. The authors have seen the powerful peristaltic waves of the stomach so propel the gastric contents out through the new opening that it was forced into all of the smaller bile passages. Another disadvantage of anastomosis of the gall-bladder to the stomach is that the wall of the stomach is thick with a loose redundant mucosa, which makes the accurate anastomosis of the stretched-out, thin-walled gall-bladder to the stomach difficult.

In anastomosis of the gall-bladder to the duodenum there are likewise disadvantages in that both structures are relatively fixed, therefore the accurate approximation and anastomosis of the gall-bladder to the duodenum may be difficult and at times a little uncertain. The gall-bladder must migrate to the duodenum since the duodenum cannot be made to migrate to the gall-bladder The rise and fall of the liver with diaphragmatic motion, which at times is of quite violent character with vomiting, must jeopardize the security of this su-Therefore, because of the difficulty at times in making this anastomosis and the danger of traction on it, the authors have entirely given up this type of operation in cases of carcinoma of the head of the pancreas

After the anastomosis between the gall-bladder and the jejunum, with its double row of sutures, is completed, a silk stitch is placed between the proximal loop of the jejunum and the capsule of the liver, close to the anastomosis,

and a similar one is placed between the distal loop of the jejunum and the capsule of the liver. This so fixes the anastomosed jejunum to the liver that it ascends and descends with any motion in that structure and thus takes all strain off the suture line. This is a most important point when one appreciates that many of these anastomoses must be made with a stretched gall-bladder wall of almost paper thinness, out of which stitches will tear very easily.

A successful resection of the head of the pancreas for a ductal carcinoma in a man 37 years of age is reported by G Crile, Jr 65 Operation was carried out in 2 stages, first a cholecystogastrostomy was performed, and 2 months later the head of the pancreas was resected

Prior to the first operation the icterus index was 100, and the blood phosphatase 66 units. The course following this operation was stormy, there was marked hemorrhage, and a septic type of temperature which was interpreted as being due to cholangitis. To control the hemorrhage, a total of 4500 cc. of blood was administered during the first 7 postoperative days.

The second operation was done under spinal anesthesia. To facilitate the procedure the gastrocolic omentum was divided along the greater curvature of the stomach. The duodenum was divided just distal to the pylorus and the latter was inverted, the gastroduodenal artery was ligated, as was the common duct, and the duodenum was mobilized from its lateral border and again severed, this time in the third portion. The hand could then be inserted behind the pancreas, which was adherent to the duodenum A finger was placed beneath the neck of the pancreas, well beyond the tumor, and the pancreas was cut across. The pancreatic duct was markedly enlarged and this, together with the pancreas, was sutured with 3 mattress sutures of alloy steel wire. The entire head of the pancreas with the tumor was lifted out *en masse* Troublesome bleeding occurred in the veins of the region. A gastroenterostomy was then performed.

The convalescence from this operation was also stormy, with hemorrhage and cholangitis again supervening. Again recourse was made to numerous transfusions (a total of 3500 cc. of blood) and to the use of large quantities of intravenous glucose.

STOMACH

Gastric Phlegmon

W. Stotz⁶⁶ gives a good picture of gastric phlegmon. The condition is very rare. Three hundred and one cases have been reported, of which 105 have been collected by the author since the compilation of Finsterer 10 years ago. This includes the 84 cases described by Melander.

Classification — The author groups these phlegmons according to the classification of Stindberg as follows: (1) The gastric phlegmon which is either diffuse or circumscribed, (2) the gastric abscess; (3) the mixed forms, (a) with one or more abscesses and (b) with more or less phlegmon

Pathology—The pathology is usually first limited to the submucosa from which the muscularis is invaded, and seldom involves the mucous membrane. Following perforation into the gastric lumen the abscess may drain from below the submucosa. The extent of the process can be determined only histologically even though macroscopically the transition from pathological to normal is very noticeable. A chronic case of phlegmon may proceed to linitis. Streptococci were

found in 79 per cent, pneumococci in 4 per cent, and Fraenkel-Welch bacilli in 1 per cent.

The primary idiopathic disease is believed to be caused by other factors, however. The earlier belief that poor hygienic factors (alcoholism) caused the condition is not correct. Racial characteristics may have some bearing: The condition is found very frequently in the Ukraine. Men are affected more often than women. The patients were most often between the third and sixth decades of life. There are 2 forms of gastric phlegmon: (1) The acute, with fever and general symptoms predominating; and (2) the subacute, a chronic form usually without fever

Symptoms—The symptoms are usually referred to the upper abdomen Preoperative diagnosis was possible in only 2 of the 66 cases seen in the last 10 years. Two cases have been reported in which such a preoperative diagnosis was made roentgenologically (Rothermel and Olsson).

Prognosis — The prognosis is bad, Sundberg reports a mortality of 92 per cent. In the author's 105 cases the mortality was 70 per cent. The prognosis is best in the chronic localized cases. The more severe the peritonitis accompanying the condition, the poorer the prognosis.

Treatment—The treatment is essentially surgical Of 30 patients treated by gastric resection, 21 survived; all of this group presented the subacute chronic localized type of phlegmon Only 1 patient with diffuse gastric phlegmon (reported by Melander) who underwent exploratory laparotomy and was treated with antistreptococcic serum and drainage, and an additional patient (case reported by von Paugger), also undergoing laparotomy and treated by omental covering of the necrotic gastric wall plus

drainage of the peritoneal cavity, have recovered. However, resection is not always the operation of choice; the surgeon must rely entirely upon the findings in each specific case. At present, treatment with *prontosil* should be considered. The author reports 2 cases of his own. Both patients died, 1 after operation, the other after exploratory laparotomy.

The term acute cellulitis of the stomach is preferred by A. Lyall⁶⁷ to phlegmonous gastritis. Seven cases reported which show that the condition is not always fatal. Recovery occurred in 2 of his cases and in 1 reported by Marshall (1935). Such healing may play a part in the etiology of gastric ulcer. He imagines that a slight degree of this cellulitis is not uncommon in association with peptic ulcer, especially one which has been showing recent acute activity and has perforated. The friability of the gastric wall around certain perforations, making the insertion of the "pursestring" suture difficult, is probably due to spread of infection for some distance round the ulcer. The danger of performing a partial gastrectomy in such cases and thus cutting across infected tissue is obvious The closure of the perforation by a plug of omentum, as in one of his cases, appears to be the safer procedure. Certain possibilities in the etiology of the condition discussed by the author are infection through a break in the gastric mucosa, poisons and hematogenic infection

Postoperative phlegmonous gastritis is reported in a patient by M. Persson ⁶⁸ Resection of the stomach and duodenum plus gastroenterostomy, Billroth II, were undertaken on a female patient, 40 years of age, with medically intractable ulcer of the duodenal bulb. Healing was uneventful and the patient was discharged 2½ weeks later. The next day, after returning home, fever, sore throat, and

prostration of influenzal character developed, and 2 days later vomiting occurred and pain was present in the right lower quadrant. The appendix at removal, 22 days after the resection, exhibited some pathological changes and there was some seromucous fluid in the peritoneal cavity, but palpation of the upper abdominal cavity through the operative incision failed to reveal any evidence of abscess

Following appendectomy the condition of the patient became worse and 2 days later, under a tentative x-ray diagnosis of subphrenic abscess, the eleventh and twelfth ribs on the left side were resected, and a large abscess, bounded by the stomach, spleen, left lobe of the liver. and diaphragm, was uncovered and drained. The stomach at this operation was swollen and thickened, and at autopsy the following day the gastric wall was found to be greatly thickened and interpocketed with turbid grayishyellow pus Culture revealed the strep-The course of the condition tococcus was as follows: Phlegmonous gastritis. subphrenic abscess, and then diffuse purulent peritonitis

This case, in view of 2 others reviewed by the author from the literature, 6 collected by Finsterer and 4 by Perman, 69 is the thirteenth reported instance of postoperative phlegmonous gastritis. The author accepts in the main the conclusions of Perman, even believing that the peculiarities of this case strikingly support that author's views as to the pathogenesis of the condition.

The long, complication-free interval following the resection renders the subsequent development of a nascent phlegmonous process unlikely, but the toxins of the anginal process would explain the presence of a hypo-acidity favoring prevalence in the stomach of virulent swallowed bacteria, which might invade the gastric wall by way of the sluggishly

healing mucosal stratum of the suture line at the gastrointestinal junction, resulting from the first operation.

As practical conclusions the author suggests the importance of preoperative mouth hygiene and of the shielding, insofar as possible, of the patient recently operated for ulcer from infections of the respiratory tract.

Peptic Ulcer

Treatment—F H Lahey and S F. Marshall⁷⁰ point out that during the past few years there has been a gradual but very definite change in the method of handling the patient with gastric and duodenal ulcer There has been the change from the situation in which opinions were divergently divided into those advocating surgery for nearly all ulcers and those advocating nonoperative measures except when urgent complications such as perforation, obstruction, or malignant degeneration occurred. There is very little disagreement today with the more modern attitude that no ulcers are primarily surgical, that all ulcers should be given a trial of nonoperative treatment, and that all patients with ulcers should have surgical treatment only as the ulcers fail to respond under the trial of medical measures. Practically everyone is in agreement with the surgical indications which the authors have frequently discussed, namely, ulcers which are intractable to medical management, those in which 2 or more gross hemorrhages have occurred in spite of good treatment, those which have perforated, pyloric obstruction which is not amenable to medical management, and gastric ulcers in which the question of malignancy cannot be definitely settled

Although the relationship of surgery to nonoperative measures have been quite definitely established, there has been lack of agreement during the past few years as to the desirability of employing conservative operative procedures such as gastroenterostomy, gastroduodenostomy, or various forms of pyloroplasty with or without the excision of the ulcer or whether or not more radical procedures such as subtotal gastrectomy should be employed

It seems to the authors that subtotal gastrectomy has now been more and more generally accepted throughout this country and England, the 2 countries in which acceptance of the method, when first advocated by continental surgeons, was most strenuously resisted

There were certain psychological reasons that made the acceptance of subtotal gastrectomy for peptic ulcer difficult for everyone It was particularly difficult for everyone to accept the plan of removing large portions of the stomach for an ulcer no larger than one's little finger nail It was particularly difficult also to accept this procedure when many of the patients with the lesion, although uncomfortable, were able to be up and about and, with the aid of alkalies and frequent feedings, to struggle through the years, suffering only periodic attacks of discomfort and disability. It was further difficult to accept this radical operative procedure because up to the time that one becomes expert with it, the mortality rate is distressing and a fatality in a patient, who is not in a condition of acute abdominal emergency, who is able to be up and around and at times at least to support himself partially, is a particularly depressing and distressing one. For these reasons it was but natural that subtotal gastrectomy, as a method of surgical treatment for gastric and duodenal ulcer, was accepted only after having met with considerable resistance and among the prominent resisters it is but fair to say that the authors themselves were included

Haberer and Finsterer, who did proneer work in Europe and in this country, and Berg, Lewissohn and Strauss deserve a great deal of credit for their persistent advocacy of this method of surgical treatment in the face of vigorous and at times almost bitter criticism.

It is being more and more accepted, as Lahey and Marshall have said, that conservative surgical procedures, such as gastroenterostomy and pyloroplasty, are lest their attitude be misinterpreted it is but fair for them to say that occasional cases will arise in which it would be unsafe and unwise to apply subtotal gastrectomy. It would be a mistake, they believe, for anyone dealing with gastric and duodenal ulcer to take the attitude that all patients with gastric or duodenal ulcer, regardless of their age, condition, weight, or location of the ulcer, should be submitted to subtotal gastrec-

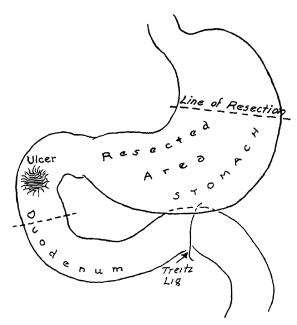


Fig. 32—Left: A diagrammatic sketch solely to demonstrate the amount of stomach and duodenum resected. (Lahev and Marshall. Surg., Gynce and Obst.)

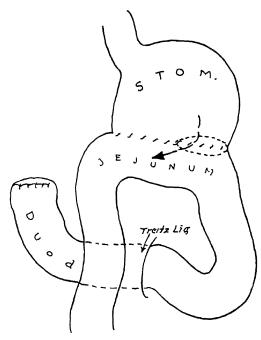
no longer justifiable as routine operations for patients with gastric and duodenal ulcer. The too frequent occurrence of gastrojejunal ulcer, so intractable to medical management, and the occasional incidence of gastrojejunocolic fistula, a lesion with a disturbing mortality rate, has led a great many surgeons to avoid the routine use of these conservative procedures

While the authors feel entirely in sympathy with the selection of subtotal gastrectomy as the method of choice in the surgical treatment of duodenal and gastric ulcer, nevertheless they think that

tomy Lahey and Marshall believe very strongly that in bad risk cases it is infinitely better to perform an operation with which one is not as well satisfied but to which is attached a lower mortality rate. The authors believe from their experience that occasionally there are patients with indurated ulcers, low in the duodenum, close to and even involving the common bile-duct, with a marked degree of pyloric obstruction, on whom subtotal gastrectomy cannot be done with safety because of the fact that there would be insufficient duodenum left for safe inversion of its end In such a patient, the operation of Finsterer here described in Fig. 37, in which the ulcer is left in place, occasionally cannot be done because of the fact that the pylorus is obstructed and the remaining stump, therefore, will not drain. Lahey and Marshall think that every patient with ulcer who is approached surgically should be considered as to the possibility of subtotal

dence of digestive difficulty after operation is also greatly lessened.

It has seemed to the authors that it would be of value to present in illustrations and legends the technic of the now relatively standardized subtotal gastrectomy to which they have come after a considerable experience with various types of operative procedures. Up to



log 33- Diagrammatic sketch of the principle of the Hofmeister procedure. Note the closure of the upper half of the transected stomach, the anastomosis established at the lower half, and the loop of the jejunum buttiessed over the upper closed half of the stomach. In this illustration the proximal portion of the jejunum is shown attached to the greater curvature of the stomach. This is occasionally done when the position of the jejunum is such that the jejunum is anastomosed to the lesser curvature of the stomach. (Lahey and Marshall. Surg., Gynec and Obst.)

gastrectomy and estimated upon the basis of his general condition, age, weight, and the location of the ulcer, and then only should the operative procedure be selected

In a follow-up study of 200 cases in which subtotal gastrectomy has been done for ulcer, it has been demonstrated that the end-results, at least so far, are superior to those obtained by the use of the more conservative procedures, namely, a gastroenterostomy or pyloroplasty. There are fewer recurrent ulcers and the inci-

September 28, 1938, they had handled 362 cases.

It has also seemed to the authors that it might be of value, comfort, and perhaps encouragement to other surgeons to report their mistakes and to state that there has been no operation in their experience in which it has been more difficult for them to overcome complications and in which it has been more difficult to reduce mortality than in that of subtotal gastrectomy

It seems to Lahey and Marshall that there is no operation in which a relatively large experience and frequent practice is more important and more necessary than that of subtotal gastrectomy if the mortality rate is to be reduced and kept low

There is no operation with which the authors have had experience in which

in relation to the ease with which the operation can be done but more particularly to complications, such as pulmonary complications, wound infections, and obstruction after operation

Anesthesia — Lahey and Marshall state that they have passed through several phases of the employment of differ-

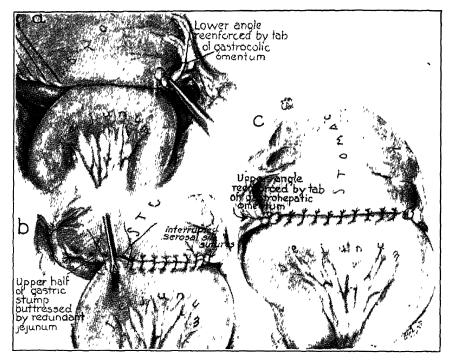


Fig. 34—a. The completed Connell catgut suture with the upper end of the stomach closed In b. the anterior row of catgut sutures is covered by a row of interrupted black silk sutures. Note the method in b of buttressing the jejunum over the upper closed half of the stomach by placing silk stitches between the posterior and anterior wall of the stomach and the jejenum, thus securely reinforcing this suture line with the buttressed jejunum.

In c the complete anastomosis is seen, the lower half is occupied by the anastomosis, the upper half of the stomach serving to buttiess the excess jejunum over the closed upper half of the transected stomach. Note also that as the last strich on the lesser curvature is fied, a tab of gastrohepatic omentum is fied in it to remforce the angle and to suspend the suture line, and in the lower angle likewise a tab of gastrocolic omentum is fied into the last lower strich to reinforce this angle. This may also be seen in the lower angle in a. This we believe has been a valuable procedure in suspending the line of anastomosis and in reinforcing the upper and lower angles (Lahey and Marshall. Surg., Gynec and Obst.)

cooperation between gastroenterologists in the preparation of the patient and in the management of the active stage of the ulcer before coming to surgery is more necessary than in this one. Certainly there is no operation in surgery of their experience in which the type of anesthesia plays a greater part not only

ent types of anesthesia. Their first operations were done under ether and it soon became evident that this type of anesthesia was not desirable, due to the length of time necessary to complete many of these complicated procedures, and due to the fact that undesirable depths of anesthesia were necessary in order to obtain relaxation sufficiently adequate to get the exposure with which to do high gastric resections. Following the abandonment of ether, they employed spinal anesthesia in the form of spinocaine. The disadvantage of this anesthesia was its inadequate time length. Often these patients under spinocaine

essary to do high sutures in the extensive resections. This combination of anesthesias, therefore, was soon given up and Lahey and Marshall turned to intratracheal ethylene combined with regional anesthesia and splanchnic block. This proved to be very satisfactory. Many subtotal and some total gastrectomies

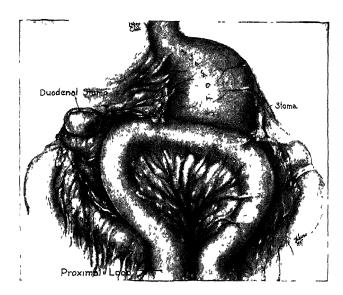


Fig 35—This shows the Hofmeister anastomosis completed. In it may be seen the closed duodenal stump, the jejunum buttressed over the upper half of the stomach, the gastrohepatic omentum tied into the upper angle, and the gastrocohe omentum tied into the lower angle of the anastomosis.

One of the purposes in presenting this illustration is to mention particularly the length of the jejunal loop necessary to approximate it to the transected end of the stomach without tension. One must realize, when the length of jejunum required is estimated, that when the anastomosis between the jejunum and the stomach is made the stomach is under tension, pulled as it is down into the wound. One must also realize that after the anastomosis is made the stomach will retract into the left hypochondrium and that if a short length of jejunum is brought up over the transverse colon to anastomose to the cut end of the stomach, when that structure retracts, the siture line may be under considerable tension. It is, therefore, very important, we believe, to pull out plenty of jejunum and then to pull out quite a little more, allowing for this retraction of the stomach into the left hypochondrium. We have seen no disadvantage in the long jejunal loop. Here the proximal loop of the jejunum is shown anastomosed to the lesser curvature of the stomach as is so frequently our custom. Note also that no jejunojejunostomy is employed. (Lahey and Marshall.—Surg., Gynec and Obst.)

would come out of their anesthesia at the end of an hour to an hour and a quarter, at the latest an hour and a half. This was particularly undesirable, since at this time many of the patients frequently had marked drops in blood pressure. In spite of this, it was still necessary to administer a general anesthesia and carry these patients into considerable depths in order to maintain the relaxation nec-

were done under this form of anesthesia While intratracheal ethylene alone did not provide sufficient relaxation for the comfortable performance of high subtotal gastrectomy, quite adequate relaxation was obtained when a regional infiltration with novocain was added, and when to this was added novocain splanchnic block, greater relaxation and less drop in blood pressure were secured.

It was not, however, until the advent of dilute nupercaine solutions, as advocated by Howard Jones, of London, that a really satisfactory anesthesia was obtained for subtotal gastrectomy. The authors have now employed dilute nupercaine spinal anesthesia in a 1:1500 dilution for about 3 years in high upper

cain. For those who have had earlier experience with nupercaine in spinal anesthesia, it is but fair to state that the early use of nupercaine anesthesia in concentrated solutions had associated with it many serious complications which have been overcome by the employment of the dilute solutions

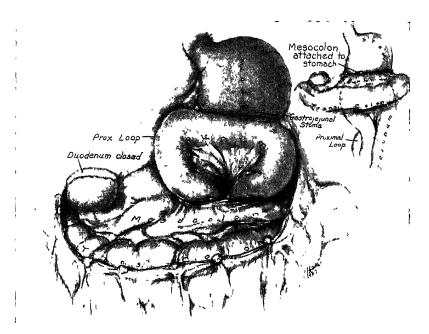


Fig. 36—Although we now prefer antecolic anastomoses of the jejunum to the cut end of the stomach, there will be cases occasionally in which, because of a short jejunal mesentery or a very thick, fat omentum, it will not be feasible to make satisfactory antecolic anastomoses. For that reason this illustration is shown depicting the method of making posterior anastomoses, and, as shown in the insert in the right upper coinci, the method of attaching the cull of the mesocolon to the stomach above the line of anastomosis to make the anastomosis within the greater peritoneal cavity. In our experience there will be cases occasionally in which it will be almost impossible to accomplish this attachment of the mesocolon to the stomach above the line of anastomosis. (Lahey and Marshall. Surg., Gynec & Obst.)

abdominal operations with complete satisfaction and it appears to be the nearly ideal anesthetic, particularly for subtotal gastrectomy. With dilute nupercaine spinal anesthesia, complete relaxation now can be obtained up to 3 or 3½ hours and even longer. There have been no undesirable complications with this type of anesthesia, and it is the opinion of the anesthetists that the drops in blood pressure are even less with nupercaine anesthesia than with the other types of spinal anesthetics, pontocaine and novo-

Technical Procedures—Before presenting the description of their technical procedures in subtotal gastrectomy, Lahey and Marshall give a few details regarding other types of operation for subtotal gastrectomy. They have occasionally employed the Billroth I type of subtotal gastrectomy. In their opinion, however, it has no place in the radical surgical management of peptic ulcer. Due to the fact that the duodenum in duodenal ulcers, which will represent the majority of the ulcers, or 9 to 1, with which they

have to deal surgically, is usually indurated and scarred as a result of the ulcer, this structure is not well adapted under these conditions for anastomosis to the cut end of the stomach. Due to the fact also that one is always interested in being able to bring the stomach over so that it can be anastomosed directly to the open end of the duodenum, there will

operation is likewise open to the same criticism due to the fact, as with the Billroth I, there is the tendency to leave sufficient stomach so that the ends can be turned in and a gastroenterostomy established between the 2. Both of these operative procedures have been entirely given up in the authors' clinic for several years.

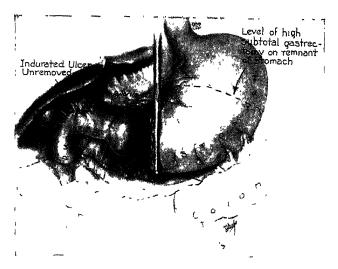


Fig 37—The method of resection by exclusion according to Finsterer. This has proved a very useful procedure for us in patients in whom the ulcer was so close to the common bile-duct that it did not seem feasible to undertake its removal. It has likewise proved valuable in bad risk patients in whom it did not seem feasible to spend the time necessary for the dissection of an indurated, adherent ulcer on the posterior wall. Note that the stomach has been cut off proximal to the pylorus and turned in , a subtotal gastrictomy will then be done up to the level shown by the dotted line. We have employed this procedure in 19 cases. It has been quite satisfactory. In 15 such patients followed the end-results have been just as satisfactory as those in whom the ulcer had been removed. One must not employ this procedure unless it is certain that there is no pyloric obstruction. Unless there is free drainage through the pylorus, fluid will accumulate in the small gastric stump and rupture the suitured end of the distal gastric stump. Failure to realize the presence of a sufficient degree of pyloric obstruction to interfere with drainage brought about the only fatality which we have had in the 19 patients in which the Finsterer resection by exclusion was applied. (Lahey and Marshall. Surg., Gynec & Obst.)

be the constant tendency to leave sufficient stomach so that this can be done, while the reverse should be true. If one is to accomplish the highest degree of relief for patients with intractable ulcer, then extensive resections of the stomach must be undertaken and there must be no hesitation or uncertainty about the amount of stomach to be removed

Early in their experience, a few of the authors' patients were managed by the Billroth II plan of procedure. This

Many of their early subtotal gastrectomies were done by the so-called Polya method, frequently spoken of in the literature as the Reichel-Polya operation. This operation has been quite satisfactory but has been supplanted for some years in their hands by the Hofmeister operation in which the upper half of the stomach is closed, as shown in Fig. 35, and the jejunum anastomosed to the lower half of the cut end of the stomach. This has, as will be discussed, the ad-

vantage of a shorter suture line and less danger of leakage

In the beginning of Lahey's and Marshall's experience with subtotal gastrectomy, the anastomosis between the cut end of the stomach and the jejunum was made with the jejunum behind the transverse colon as a posterior anastomosis This necessitates the suture of the mesentery of the colon about the stump of the stomach in order to make the anastomosis between the end of the stomach and the jejunum rest in the greater peritoneal cavity. When subtotal gastrectomy is sufficiently high so that an adequate amount of stomach is removed, it is impossible in many cases to suture the rent in the mesentery about the stomach satisfactorily and without angulation of the colon For that reason, Lahey designed and published a method of posterior anastomosis whereby the proximal loop of the jejunum was transplanted above the mesocolon with but I loop of the jejunum passing through the rent in the mesocolon, thus cutting down the danger of obstruction to the proximal or distal loop. For the past few years posterior anastomoses have largely been given up and, as will be shown in the operative illustrations, practically anastomoses between the cut end of the stomach and the jejunum are now made antecolic in location. This has distinctly lessened the incidence after operation of obstruction to the loops of the jejunum going to the stomach

Early in the authors' experience when the jejunum was brought over the transverse colon in the antecolic position and has been anastomosed to the cut end of the stomach, entercenterostomy was done between the loops. This additional step to the operation was employed because it was feared that obstruction might occur at the point of anastomosis of the jejunum to the stomach. That has been

given up entirely for some years and antecolic anastomoses with long loops of the jejunum are done with no enteroenterostomy The reasons for this are that it has been definitely proved to the authors that enteroenterostomy is not necessary and is even undesirable. If the purpose of subtotal gastrectomy is to remove the largest amount of acid-bearing glands and to cause to flow into the stomach the alkalme upper jejunal contents for neutralization of any remaining acidity, then the addition of an enteroenterostomy to a subtotal gastrectomy with antecolic anastomosis will sidetrack the alkaline jejunal contents into the jejunum, when it would be more desirable for these alkaline contents to flow into the stomach and there further neutralize acidity

In the beginning of Lahey's and Marshall's experience with subtotal gastrectonly the operative procedure was conducted with clamps upon the stomach to prevent soiling. For a number of years now all subtotal gastrectomies have been done with no clamps whatever. When one attempts to apply clamps well up under the left costal margin, the application of these clamps will of necessity limit the height to which the resection can be done, and, if the clamps are applied and the stomach then cut off, because of its high location, there will not infrequently be slipping of the clamps and spilling of the contents. Based upon their experience with these cases, the authors do not believe that it is possible to do adequately high subtotal gastrectomies, as shown in the roentgenograms of patients who have had subtotal gastrectomies, unless these operations are done without clamps or with a special procedure done with special clamps, as, for instance, the Shumaker clamps

The accompanying illustrations, with their legends, so graphically illustrate the

technic of the operative procedure that additional description is unnecessary.

Mortality—It is the authors' opinion that an operation of this magnitude should not be discussed without presenting the mortality rate which has occurred in a series of cases. Up to September 28, 1938, 200 subtotal gastrectomies for ulcer have been done Up to $2\frac{1}{2}$ years ago, the mortality was 18 per cent, by far too From $2\frac{1}{2}$ to $1\frac{1}{2}$ years ago, the mortality dropped to 11 per cent, which was still too high. For the last year and a half the mortality has been zero. Lahey and Marshall have now done radical subtotal gastrectomy upon 51 consecutive patients without a single death these are not selected cases is evidenced by the fact that out of 3500 ulcer patients treated in the clinic, only 8 per cent of the patients with gastric ulcers were submitted to surgery. In order that there may be no misunderstanding about these figures, every one of these patients had been submitted to prolonged medical treatment which failed to relieve symptoms, all of the ulcers were posterior wall-eroding ulcers, and included in these 51 cases were 8 gastrojejunal ulcers which necessitated resection of the jejunum as well as the stomach, and 1 gastrojejunocolic fistula which involved not only resection of the stomach and the jejunum but also resection of the terminal ileum, ascending colon, and right half of the transverse colon

Juxtacardiac Gastric Ulcer—
H lensterer⁷¹ maintains that the juxtacardiac ulcers hold a special position not only because of their relative rarity but also because their diagnosis and treatment are rather difficult. In a critical analysis of the results which he obtained in the surgical treatment of juxtacardiac ulcers he finds that the mortality rate was comparatively high in his material because, in some difficult cases in which

the resection of the ulcer was forced, Madlener's operation should have been done. To reduce the acidity in juxtacardiac ulcers. Madlener removes the distal half of the stomach together with the pylorus but leaves the ulcer untouched and makes the anastomosis with the duodenum according to the first method of Billroth. Finsterer says that in the future he intends to resect the ulcer only if by gastrotomy and by intragastric palpation it has been determined that the ulcer is far enough removed from the esophagus that a secure closure of the gastric stump can be obtained. For all other cases he recommends Madelener's operation, which permits a reduction in the surgical mortality and also insures better permanent results than does simple gastroenterostomy. The latter method should be employed only in exceptional emergencies The author thinks that in the interest of the patients it is better to perform Madelener's resection too often than not often enough in cases of juxtacardiac gastric ulcer

Complications of Peptic Ulcer — Hemorrhage—The treatment of bleeding peptic ulcer is one requiring considerable experience and a nicety of judgment in the handling of these cases. The problem of treatment is certainly not whether hemorrhage should be treated by medical or surgical methods, but is the determination of what system of management for each individual case will result in as few deaths as possible from this serious complication of ulcer questionably, there is a small group of patients with bleeding ulcers who must come to surgery and whom operation Jone can save However, it is the opinion of Samuel F. Marshall and Everett D Kiefer⁷² that the majority of cases can be handled conservatively without the necessity of applying surgery.

The method employed in the Lahey Clinic by the authors in the conservative treatment of hemorrhage from ulcer consists of a régime which has been generally accepted and practiced for a number of years. It is essentially an expectant and conservative régime consisting of rest in bed, morphine in doses large enough to produce adequate sedation, starvation for 2 or 3 days and then a gradual application of the Sippy diet.

In recent years the most important new therapeutic measure has been blood transfusion, but there has been lack of general agreement as to its value. Many clinicians feel that there is a distinct danger in the giving of a blood transfusion on the basis that a possible rise in blood pressure may produce a blow-out of the thrombotic plug in the bleeding vessel, causing secondary hemorrhage.

In this clinic, blood transfusions have been used rather more freely than elsewhere for 2 distinct indications: First, to correct the acute loss of blood volume: and second, as a treatment of secondary anemia merely to shorten the patient's convalescence from a severe blood loss Patients who die suddenly from the first outpouring of blood are rarely in the hospital and consequently the question of transfusion does not arise. The usual severe case of hemorrhage admitted to the hospital ward is the patient who has survived the shock of a severe blood loss. but who still presents the clinical picture associated with a marked reduction in blood volume below normal. Although life is being maintained, there are 2 distinct dangers associated with this condition. The first is danger of a secondary hemorrhage which in some cases is possible even though the blood pressure may be markedly lowered If this occurs in the case of an already markedly reduced blood volume, the additional loss of blood may be suddenly fatal The second, and what is probably the most important danger, is the effect upon function and possibly irreparable damage which takes place in vital organs as a result of long-continued reduction of blood pressure and blood volume. One of the most outstanding laboratory evidences of this is the high nonprotein nitrogen frequently found associated with severe hemorrhage; this in some cases actually appears to be important in the cause of death. The brain, heart and liver are probably also affected, but this is not so easily demonstrated in the laboratory

It would seem, therefore, that the danger of causing a secondary hemorrhage by giving a blood transfusion is distinctly less than the danger associated with letting the patient's condition remain at a low level too long. It has been the authors' experience that a small or moderate size transfusion of citrated blood given slowly by the drip method has been safe and of distinct value. They have not seen a sudden rise of blood pressure following transfusions, but they have seen the gradual rise of blood pressure from a dangerously low level, that is below the systolic pressure of 90 mm.

The decision as to whether a transfusion is indicated or not cannot be based upon the examination of the blood count, since blood volume can be reduced to a dangerously low level without making an appreciable change in the red blood count or the hemoglobin determination The changes in these values do not take place until after the blood volume has been at least partially corrected by dilution with blood fluids. Clinical estimation of the patient's condition depends upon the pallor of the skin and mucous membranes, the rate and quality of the pulse and upon the blood pressure, with additional consideration given to the estimated quality of blood that has been expelled No arbitrary rule can be followed, but a fall in systolic blood pressure to 90 mm. or below and a rise in pulse rate to over 130, particularly when there has been definite evidence of a large amount of blood loss, are indications for a transfusion.

The same criticisms may be applied to the use of intravenous and subcutaneous injections of glucose or saline solution. They are useful, however, when dehydration is severe and apparently they do allay thirst to some extent during the starvation period However, patients who are well morphinized do not complain much of thirst as a rule. If intravenous fluids are introduced slowly. the blood volume may be increased without appreciably raising the blood pressure, but on theoretical grounds at least, this is less desirable than by means of a transfusion, since the viscosity of the blood is decreased and there may be a disturbance in the clotting mechanism brought about by the dilution

Diet in the treatment of hemorrhage in peptic ulcer in this clinic and until recently generally accepted as a timehonored method of treatment consisted of starvation or the elimination of both food and water for a period before the gradual institution of the Sippy type of ulcer régime In 1933, Meulengracht upset all previously conceived ideas as to the treatment of gastrointestinal hemorrhage by reporting that he obtained a marked reduction in mortality by beginning liberal and early feeding during or immediately after the bleeding. It was his opinion that early feeding preserved the strength and nutrition in a patient and brought about a more rapid convalescence and in this way reduced the mortality figure. He reasoned that the food had therapeutic value in neutralizing the gastric acid, thereby favoring healing of the ulcer and preventing digestion of the clot in the bleeding vessel. His diet con-

sists of meat, fish, puréed vegetables, bread and butter, cheese, tea, and cereals. In 1935, he reported 251 cases of hemorrhage taken to be due to genuine ulcer with only 2 deaths; a mortality of less than 1 per cent. He did not give his criteria as to the severity of the hemorrhages nor do the authors know from his report anything of the factors which might influence the relative incidence of severe and mild cases. He does not compare his results with those of Christiansen and another hospital in Copenhagen, which appear to have an identical type of case, and treated in the orthodox way. In this group there was a mortality of 7.9 per cent in 289 patients.

Meulengracht's report has attracted wide attention and many clinics have modified their treatment of hemorrhage along these lines, but as yet there are few reports which give the results of any sizable series of cases. In the Lahey Clinic, they have not yet changed over to the Meulengracht method of treating hemorrhaging cases, although in principle they follow his ideas to some extent They do not starve the patients for any extended number of days, although it is the authors' opinion that for 48 to 72 hours after a diffuse hemorrhage the stomach should be put at rest as nearly completely as possible. It is indeed a rare patient whose nutrition would suffer seriously from a starvation period of this length. If at the end of 2 or 3 days there is no evidence of a repetition of bleeding, it seems highly desirable to start therapeutic measures directed toward neutralizing gastric acidity, promoting healing of the ulcer. Although Meulengracht reported a 1 per cent mortality rate, it probably does not represent uniform results to be expected from this type of treatment Yet, it is significant that he has observed a very definite and

marked reduction in his mortality following this radical change in treatment

Alkalis and other forms of antiacid therapy should be used as in the routine management of an active ulcer. Starting the régime, however, it is necessary to observe precautions to avoid overloading the patient with too large a volume of food and medicine. The treatment of the secondary anemia should not be delayed, and the patient's convalescence can be hastened by the administration of sufficient iron. The authors have used chiefly ferrous sulfate in doses of 6 grains (0.39 Gm.) 3 times a day

Morphine is the drug most commonly used for sedation in dosages of \(^1/6\) to \(^1/4\) grain (10 to 16 mg) every 4 hours, depending upon the quantity necessary to keep the patient immobile and asleep most of the time. The patients who react to morphine with nausea and vomiting and nervous irritability may be given hypodermic medication of soluble barbiturates in dosages sufficient to obtain the desired results.

There has been some reported evidence suggesting a relationship between subclinical avitanimosis C and bleeding ulcer, but the importance of this relationship is still unsettled. In cases which show definite increase in capillary fragility above normal, *vitamin C* medication given parenterally would seem to be indicated. At present there is little evidence that the resistance of the blood vessels can be increased above normal by the administration of vitamin C. Furthermore, severe bleeding in peptic ulcer is not usually a capillary type of bleeding

The use of hemostatics, vasoconstrictors and astringents has fallen into disrepute, and there is little on either theoretical or clinical grounds to support their use. The hemorrhage in pepticulcer is not caused by failure of the blood to clot, but is due to the mechanical

opening of the vessel Furthermore, there is always the danger that the administration of such medication may cause vomiting or other disturbances which are distinctly detrimental to the cessation of bleeding.

Clinical decisions in any given case of severe hemorrhage must be based upon an estimation of the disease present, upon knowledge of all the factors which influence the prognosis and an accurate appreciation of just what can be accomplished in the way of treatment, whether it be medical or surgical. Nearly all of the severe and fatal cases of hemorrhage in duodenal ulcer occur from large posterior wall adherent ulcers with erosion of the pancreaticoduodenal artery Hemorrhage which occurs in a longstanding chronic ulcer is apt to be serious, since the abundant scar tissue interferes with the retraction of the eroded end of the Large gastric ulcers situated on the posterior wall and eroding into the pancreas also give rise to the most severe type of hemorrhage. Hypertension and arteriosclerosis are complicating factors which tend to aggravate hemorrhage. In hypertension the unduly elevated blood pressure may dislodge the clot repeatedly, and in arteriosclerosis there is loss of retractility of the vessel walls. The influence of sex and age upon the prognosis of gross hemorrhage has been repeatedly pointed out. Many authors have observed that the mortality in patients over the age of 45 or 50 is 4 or 5 times that of patients below this age. It has also been noted that women rarely die from hemorrhage in ulcer In Lahey Clinic and in several other clinics, there has not been a fatality in women from such a cause

Adequate and intelligent nursing care is essential to keep the patient at rest and to watch for signs of further bleeding. Hourly observations of the pulse

rate and blood pressure are particularly useful. A sudden fall in blood pressure, a rise in pulse rate or other signs of collapse must be interpreted as indicating secondary bleeding even though there is no hematemesis or inclena

In the authors' experience, the occurrence of signs and symptoms indicating recurrent or secondary hemorrhage while the patient is on a complete hemorrhage régime is a serious omen and is an extremely important prognostic sign. When there is recurrent hemorrhage while under treatment, particularly if it is accompanied by signs of shock, it indicates that a large artery branch has been opened and that the retraction of the eroded ends of clot formation is madequate. When this occurs in a patient who has had a long history of a severe ulcer. and who probably has a chronic indurated duodenal lesion, particularly in a male over the age of 50, the significance of this clinical course is emphasized

When it is obvious with continuation of bleeding that a large artery is the source of bemorrhage or when continuous drip transfusion or repeated transfusion has failed to control the bleeding or to keep the blood pressure at a reasonable level it is then apparent that immediate operation may prove to be necessary to prevent a fatal outcome

The decision for employing surgery in a case of bleeding ulcer is a serious matter and requires the utmost co-operation between the internist and the surgeon Certainly, early consultation between the internist and surgeon is a most desirable feature and it should be emphasized that this consultation should not be delayed until operation is recommended on the basis of a last desperate effort to save the patient's life. There can be no question that it would be distinctly wrong to advocate operation for the treatment of acute massive hemorrhage occurring from

all gastric and duodenal ulcers Should such a course be followed, it would result in many deaths. The authors certainly would not advocate or recommend that all patients who have bleeding from peptic ulcers should have operation within 48 hours For such a policy to become widespread or in general use as advocated by some surgeons would be serious indeed. Certainly such surgery should be carried out only by surgeons having considerable experience in gastric surgery and in large hospitals which are sufficiently equipped to permit emergency surgery of that character to be performed with reasonable safety Furthermore, a sufficient number of donors should be at hand to provide any amount of blood that may prove to be necessary to the patient during such an operation

Lahey has described 2 distinct types of acute hemorrhage occurring in patients with peptic ulcer and the recognition of these types has proved of great practical benefit to the authors in determining which case may possibly require surgical intervention. The first and more frequent type is that in which a single hemorrhame occurs, evidenced by the vomiting of blood or by passing a large tarry stool. in conjunction with varying degrees of shock. The hemorrhage may continue or may be repeated during the following 24 or 36 hours, but with the application of conservative medical measures the bleeding ceases and does not recur. With this type surgery will not prove to be necessarv

There is another type of massive recurrent hemorrhage in which large amounts of blood are lost by vomiting or by stool, in which the hemorrhage is continued or repeated again and again on the same day or during the following days, in which serious blood loss is evident by a fall in blood pressure, which is uncontrolled by repeated blood transfusions or

continuous blood drip. It is obvious that unless something can be done early, fatality will certainly result.

There is danger in delay in such a case, and it is generally accepted that the mortality in surgery mounts rapidly as the patient becomes more and more exsanguinated. If it can be definitely established that the patient is having recurrent gushing hemorrhages in spite of a complete and adequate medical régime, transfusions and operation should be done. It would be highly desirable if this type of patient could be operated upon within 48 hours of his first hemorrhage, but it is scarcely possible to do this in all cases and still allow time to determine whether or not he is having secondary hemorrhages. The authors entirely agree with Finsterer, who is the chief advocate of surgical treatment for acute hemorrhage, in his practice of operating upon all patients who have passed middle age who have a severe hemorrhage, even though his reported mortality in early operations compares very favorably with the medical mortality in this group of cases. It seems very unlikely that Finsterer's low mortality rate of 5.1 per cent could be duplicated by more than a very few surgeons

Such serious hemorrhages usually result from an erosion of the pancreaticoduodenal artery at the base of a penetrating ulcer of the posterior wall of the duodenum, or an erosion of the left gastric artery or of the gastro-epiploic artery in a gastric ulcer on the posterior wall of the stomach which may perforate into the body of the pancreas This type of hemorrhage usually occurs in a patient with chronic callous ulcer with rigid ulcer base In the majority of cases, the patient is a male over 50, with sclerotic arteries. Too early and ill-considered surgical interference in these cases cannot be too heartily condemned.

Surgical interference should be designed primarily to control hemorrhage and except in a few cases need not include removal of the ulcer or be designed to effect permanent cure of the ulcer condition.

If the patient's condition is such, if the experience at hand is sufficient, and if the equipment is adequate to proceed with more radical surgery, the authors believe that removal of the ulcer with a high resection of the stomach of the Hofmeister type should be carried out. However, in conditions where such an extensive surgical procedure would be very likely to result in a fatality, a more conservative method of handling the situation should be employed

Gastroenterostomy alone is not a satisfactory operation to control bleeding from an ulcer and is rarely used or advised. The effect of such a procedure in controlling hemorrhage is an indirect one because it presumably places the pylorus and duodenum at rest and permits continuous emptying of the stomach through the gastrojejunal stoma.

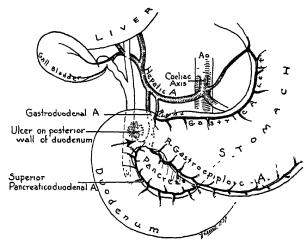
The majority of patients with severe hemorrhage requiring surgical interference will be found to have bleeding from arteries of large caliber such as the pancicaticoduodenal or other arteries which so abundantly anastomose about the head of the pancicas

The type of ulcer which is associated with much induration, with extensive periduodenal adhesions, makes simple ligation of the main trunks of the arteries supplying the pylorus and duodenum a difficult and most uncertain procedure (Fig. 38). To ligate the right gastric artery or the gastroduodenal artery may not be sufficient to establish hemostasis and fatal hemorrhage may result from the numerous anastomoses of arteries about the head of the pancreas.

In the case of hemorrhage resulting from a duodenal ulcer, if the patient's condition does not warrant a removal of the ulcer, with a high resection of the stomach, it is the practice of the Lahey Clinic to proceed with a transduodenal ligation, with silk transfixion sutures, of the bleeding vessels and to accompany this procedure in most cases with a gastrojejunostomy.

the duodenum, extending through and above the pyloric ring; all bleeding points are ligated and a pyloroplasty is made by closing the incision transversely.

However, when the hemorrhage results from a deeply penetrating ulcer on the posterior wall of the duodenum the superior and inferior borders of the duodenum and pyloric area are grasped by tacking forceps and an incision is



 $\log 38$ —The arterial blood supply of the pyloric area of the stomach and duodenum. The relationship of a posterior wall duodenal ulcer to large arteries is noted. (Marshall and Kiefer Am. J. Surg.)

The method of procedure is as follows. A high left rectus incision is made, of sufficient length to permit ready exploration of the upper abdomen. The situation of the ulcer which is the source of hemorrhage is readily determined in the majority of cases by examination of the stomach and duodenum. In an occasional case it may be difficult to determine the presence of an ulcer on the posterior wall of the duodenum and incision of the anterior wall of the duodenum may be required to demonstrate the source of the hemorrhage.

Should the blood be issuing from an anterior wall lesion, this would be obvious upon inspection and in the majority of cases such an ulcer can be excised by a longitudinal incision along the axis of

made into the duodenum and extended above the pylorus for about an inch, opening the duodenum widely duodenum and stomach are aspirated to avoid spilling stomach contents, and the source of the hemorrhage can be easily determined In most cases the blood will be seen to be issuing from an artery of large caliber at the base of the ulcer. The bleeding may then be controlled by mattress sutures of heavy silk introduced into the posterior wall of the duodenum (Fig. 39) and including the edges of the ulcer base The authors advise the employment of a nonabsorbable material for this suture because with 1 patient they had recurrence of hemorrhage 10 days after ligation, due to the digestion of the catgut suture material In this

case reoperation with removal of the ulcer-bearing area of the duodenum and a high resection of the stomach was completed, with recovery of the patient.

Following the ligation of the ulcer base, the rent in the duodenum and pyloric area is closed transversely, thus performing a typical pyloroplasty. In the event of considerable scarring and concause of the patient's condition, a simple excision of the ulcer with closure of the opening in the stomach is performed. In this event a posterior gastroenterostomy is always employed to avoid interference with gastric emptying.

However, if the patient's condition following massive blood transfusions before and during operation permits resection

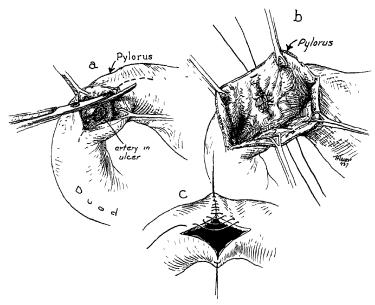


Fig. 39—Transduodenal ligation of bleeding vessel in ulcci on the posterior wall. a, meision opening the duodenum extended past the pylorus for about 3 cm., b, mattress sutures of silk are introduced through the base of the ulcci to control hemorrhage, c, pyloroplasty performed by closing the meision transversely. (Marshall and Kiefer. Am. J. Surg.)

traction of the duodenum with resultant narrowing of the lumen, a posterior gastrojejunostomy is always employed

If, however, upon exploration examination of the stomach and duodenum discloses the hemorrhage to be issuing from a gastric ulcer on the posterior wall of the stomach which has penetrated into the pancreas, the stomach is freed from the pancreas and from the base of the ulcer, the bleeding vessels are ligated, the margins of the ulcer are excised from the stomach wall, and the rent in the stomach is simply closed by suture without gastroenterostomy. If the ulcer proves to be on the lesser curvature and resection is considered impossible be-

of the stomach, the authors prefer to remove the ulcer, whether duodenal or gastric in origin, and proceed with a high resection, that is, removing with the ulcer three-fourths to four-fifths of the stomach and performing a gastrojejunostomy of the antecolic Hofmeister type (Fig. 40). It is evident that the conservative operative procedure such as outlined above may fail to relieve ulcer distress permanently, or prevent recurrent hemorrhage. Permanent relief is more apt to follow a high resection of the stomach with removal of the ulcer area, but this is not always possible because of the serious condition of the patient at the time that operation is carried out Certainly if conservative operative methods are employed and if the patient has a recurrence of symptoms upon a good ulcer régime a high resection of the stomach should be advised and carried out as early as possible

In preparation for such an operation a method for infusion of blood into the patient to control blood pressure and partially to restore blood loss must be provided for Immediately before operation a Hendon cannula is tied into the long internal saphenous vein in the ankle and during operation a continuous drip transfusion of blood is given. This method has proved thoroughly reliable and satisfactory:

The type of anesthesia employed in these cases is a regional block of the abdominal wall, obtained by infiltration with 0.25 per cent novocain solution, which may be supplemented, if necessary, with a light cyclopropane gas anesthesia Cyclopropane gas oxygen anesthesia is of especial value to supplement regional block because of the high oxygen concentration (80 to 85 per cent) which may be desirable in view of the anemia resulting from blood loss. If the patient's blood pressure is controllable at a reasonable level by the rapid infusion of blood and his condition is reasonably good, the authors prefer to employ a dilute nupercaine solution 1 1500 dilution, as a spinal anesthetic This form of spinal anesthesia can be safely employed in most patients and is a much more adequate anesthesia in the event that a high resection of the stomach with removal of the ulcer can be used in the particular case

In summarizing, the authors state that acute massive hemorrhage from peptic ulcer is a serious complication, particularly in patients with chronic, callous ulcer

In a series of 108 cases of massive hemorrhage of peptic ulcer in the Lahey Clinic, there were 5 deaths, a mortality of 46 per cent

In the majority of cases the method of treatment employed in acute hemorrhage from peptic ulcer is a conservative régime consisting of **rest in bed, morphine** in doses large enough to produce

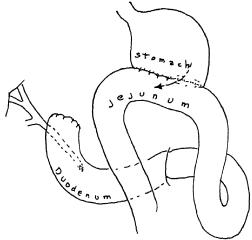


Fig 40—Subtotal gastrectomy, Hofmeister method. The ulcer is removed and high resection of the stomach is done. The jejunum is brought anterior to the colon. The gastrojejunal stoma is indicated by a dotted line. This is the operation of choice for bleeding ulcer if the patient's condition will permit (Maishall and Kiefer. Am. J. Surg.)

adequate sedation, **starvation diet** for a few days, and then a gradual application of the **Sippy régime**

Surgical management is employed in a very small group of cases in which there is continuous bleeding from an erosion of a large caliber vessel, uncontrollable by conservative measures

The operation of resection of the stomach with the removal of the ulcer is the operation of choice, provided the patient's condition will permit it. If resection cannot be employed, a more conservative procedure is followed, such as transduodenal ligation of the eroded vessel in duodenal ulcers, or an excision of a gastric ulcer, with or without a gastroenterostomy.

Perforation—The subject of peptic ulcers perforating into the pancreas is given by J. S. Horsley ⁷³ He states that a peptic ulcer that has perforated into the pancreas presents quite a different clinical and pathologic picture from an ulcer that has not so perforated. It always gives a history of previous gastric disturbance, which may be long or short.

Relief by food, soda or vomiting is not constant and there is a sense of discomsphincter gives added symptoms of discomfort and obstruction because of the spasm of the sphincter and local edema Roentgenologic examination is not always convincing, especially if the ulcer is within the grasp of the pyloric sphincter.

The pathologic picture also changes, because, in addition to the lesion in the stomach, there is some degree of pancreatitis. The pancreatitis is usually

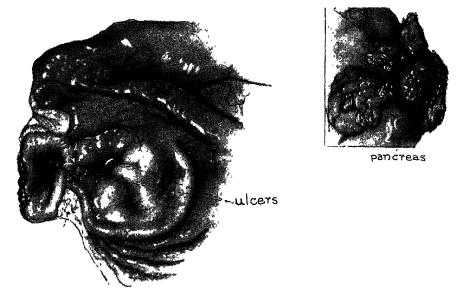


Fig. 41—Path No. 12831. λ V. H. white, male, age 52. Operation April 27, 1937. Specimen of the stomach measured 16 cm. along the lesser curvature and 25 cm. along the greater curvature. On the posterior surface of the stomach near the pyloric sphinter was some adherent panciente tissue which was dissected off with the cautery. The stomach showed evidence of gastritis and there was a pouch, probably resulting from a preceding pyloroplasty. There were 2 peptic ulcers, 1 in the stomach and 1 in the duodenum. (Horsley: Ann. Surg.)

fort and a tenderness on pressure in the upper abdomen which was not present before the perforation. When the perforation actually occurs pain may be severe.

Medical treatment after the perforation is not so effective as before the perforation. There is also considerable danger of bleeding. The vascular tissues of the pancreas tend to bleed quite freely, particularly if the perforation is large, and the hemorrhage may be profuse. A posterior perforating ulcer of the pyloric local around the region of the perforation, but it may become more extensive Unless it spreads, the associated local pancreatitis gives no symptoms of a disturbed function of this gland and laboratory tests are futile. The pain is often referred to the back, either to the right or to the left of the spine, and is occasionally so intense as to resemble the pain caused by a stone in the kidney, by nephralgia, or by acute cholecystitis. The previous history of the patient with peptic ulcer should aid much in the diagnosis of the subsequent events when there is perforation into the pancreas.

Not infrequently, in cases of persistent pain or discomfort unrelieved by medical treatment when a peptic ulcer has been demonstrated in the anterior wall of the duodenum, there exists in the posterior wall another ulcer that has perforated into the pancreas. One should not be deceived, then, by an ulcer in the anterior wall of the duodenum into thinking that it is the only lesion

During a period of 10 years, from December 31, 1928, to December 13, 1938, the author has operated upon 20 cases of peptic ulcer of the stomach or duodenum that had perforated into the pancreas In all of these cases a partial gastrectomy was performed, in 18, by modification of the Billroth I type described elsewhere, in which the upper border of the stomach is united to the upper border of the duodenum and the duodenum is flared open In 2 cases this operation could not be applied, and a Hofmeister modification of the Billroth II type was performed

Nine of the ulcers were duodenal, 9 were gastric, 1 was a duodenal-jejunal ulcer, and in 1 case there were both a duodenal and a gastric ulcer. Five of the gastric ulcers were within the grasp of the pyloric sphincter.

Treatment—The technic used in all but 2 of these cases is essentially the same as that previously described in several publications. It is a modification of the Billroth I type of operation in which the lesser curvature of the stomach is aligned to the upper border of the duodenum, and the duodenum is flared open to prevent obstruction However, the procedure has to be altered somewhat in After dividing and individual cases tying the segments of the gastrocolic omentum from the point of the proposed resection to the pylorus, and the vessels

along the lesser curvature in the gastrohepatic omentum, the portion of the stomach to be removed remains attached only by its two ends and by the adherent ulcer. Two Payr clamps are placed on the body of the stomach, which is divided between them with an electric cautery.

Usually the lesion will prevent the placing of a clamp on the duodenum. The stomach is then lifted up, and, with a very hot electric cautery, the adherent pancreas is shaved off as a thin slice. care being taken not to open the ulcer. This can best be done by approaching the adherent region carefully and freeing it to some extent on each side. Too much of the pancreas should not be removed. If the ulcer is accidentally opened, the opening is plugged with wet gauze or the finger is inserted into it. Then, with tension on the stomach, the rest of the adherent strip of pancreas is cut off. If the cautery is quite hot and the stomach is lifted up, a thin slice of the pancreas can be quickly removed without burning one's finger. If the ulcer is in the stomach, after freeing it, the duodenum is separated from the pancreas and cut across with the cautery, catching the margins of the duodenum as the incision is made. The duodenal contents are removed with a suction apparatus and a sponge moistened with salt solution is gently placed in the duodenum. If the perforation is from a duodenal ulcer, the base of the ulcer is shaved off in a similar way. The operation here is somewhat more difficult because of shortness of the stump of the duodenum, but this technic can be carried out, probably more satisfactorily, in these cases than the Billroth II type of partial gastrectomy if the ulcer is removed, because with a very short stump of the duodenum resulting from the excision of the ulcerated area it becomes difficult to close the stump of the duodenum effectively. If

there is back pressure, which occurs not infrequently after the Billroth II operation, a duodenal fistula may result, whereas in this type of operation the posterior wall of the stump of the stomach is tucked in by the short posterior wall of the stump of the duodenum and sutured. This makes the situation in this region comparatively safe because the

which is usually accomplished by the insertion of a Jutte or Levine tube into the stomach through the nose. In some patients the presence of the tube is quite a nuisance. If it stays in constantly for a few days it often irritates the nose and throat, and if it has to be inserted every few hours, the repeated insertions are even more disagreeable than having the

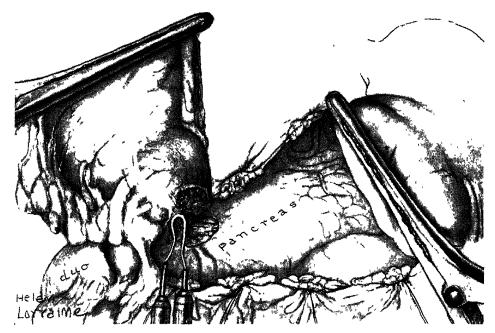


Fig. 42—The stomach has been divided between 2 Pavi clamps and the distal end is lifted up while the slice of pancreatic tissue which torms the base of a penetrating ulcer is being shaved off with the hot electric cautery. (Horsley: Ann. Surg.)

wound in the pancieas has been made with the cautery and is sterile, and the peritoneum on the posterior surface of the stomach will readily unite to the short posterior stump of the duodenum and the denuded pancreas. Then, too, this sutured area is over the solid surface of the pancreas, and if there is not an accurate healing at this point the charred and sterile pancreatic wound will act as a bumper of safety

11 Stab Wound Gastrostomy—To give the stomach postoperative rest, it is essential that the contents of the stomach be removed and the dilatation prevented. tube remain. Recently, the author has employed a gastrostomy, which is much more comfortable to be patient and more efficient for dramage than the nasal tube. This is done as follows:

After the posterior row of sutures uniting the stomach to the duodenum is placed, a sharp-pointed hemostat is thrust (directly, not obliquely) through the stomach from within outward at a point on its anterior wall near the greater curvature, where the stomach can be easily brought into contact with the abdominal wall. A soft rubber catheter, No. 18, in which an additional perfora-

tion has been made near the end, and which is clamped at its middle, is caught with the hemostat and drawn into the stomach. After 3 or 4 inches of the catheter are within the stomach, the catheter is fastened to the gastric wall by a suture of fine chromic catgut and a purse-string suture of chromic catgut is placed around it. The butt of the catheter is drawn through a stab wound in the abdominal wall, and then clamped, and the clamp on its middle is removed The catheter is gently pulled upon until the stomach is in contact with the parietal peritoneum Sutures of the chromic catgut are placed between the stomach and the parietal peritoneum and some omental fat is brought around this point of contact The fat not only adds to the security of the punctured wound, but may prevent a subsequent tight adhesion.

By this method the muscular layers of the stomach are not cut, as would occur if a knife were used to make the puncture, their fibers are merely pushed apart as are the muscular bundles of the abdomen in making a McBurney incision. The catheter fits in snugly, and there is usually no leakage after the eatheter has been removed.

There seems to be some danger of rather extensive pancreatitis from an ulcer that has perforated into the pancreas. With the base of the ulcer consisting of pancreatic tissue, if the operation is delayed too long it may well be that the residual pancreatitis will not clear up promptly

The advantages of this procedure are that. The ulcer is removed along with the superficially infected portion of the pancreas, the stomach empties physiologically into the duodenum, which is more resistant to the gastric juice than the jejunum, the region of trauma is limited to 1 field, and if there is a recurrent ulcer a posterior gastroenter-

ostomy can readily be performed. A primary gastroenterostomy, which leaves this lesion *in situ*, does not appear to be logical, though there may be circumstances in which it is the only operation indicated, as when the reaction around the ulcer is extensive.

The mortality rate should not be great. In these patients, in which this type of operation has been performed, there has been no operative death. The only death following operation was in a patient in whom this procedure was not possible because of the extent of the ulcer. The ulcer could not be excised, and the Hofmeister-Billroth II type of operation had to be performed.

A simple method of making a gastrostomy to substitute for using the nasal tube is described

Repeated perforations of gastroduodenal ulcers is discussed by J. Gosset, et al 74 The authors state that in view of the rarity of reports on repeated perforations, they were at first under the impression that this is an exceptional accident After describing the clinical histories of two patients with repeated perforations, whom they recently observed, the authors say that in the literature of recent years they have found 64 cases of repeated perforations of gastric or duodenal ulcers, disregarding, of course, the perforations of postoperative jejunal ulcers, which are comparatively frequent

They admit that they are unable to estimate, even approximately, the incidence of repeated perforation but point out that Pearse observed 33 repeated perforations among 4183 cases of perforated ulcers (about 1 in 145 cases). Other authors observed 2 in 227 cases, 1 in 120, 1 in 78, 2 in 90, and 4 in 82. These figures indicate that this complication is far from being exceptional. Discussing the pathogenesis of repeated.

perforations, the authors point out that it has been suggested that they are especially frequent after simple sutures. However, others have shown that this can be explained by the fact that simple suture is the method most frequently employed in the treatment of the first perforation and that on the whole the percentages correspond to those of the diverse technics employed.

Regarding the seriousness of the repeated perforations the authors say that it is estimated diversely by different authors, some considering it as extremely grave and others as more benign than the first perforation. Pearse, for instance, reports a mortality as 9 per cent for the repeated perforations as compared to 27 per cent for the primary perforations. To explain the latter figures it has been suggested that the peritoneum developed a sort of local immunity after the first perforation. Discussing the treatment in cases of repeated perforations, the authors say that it does not differ from the usual treatment of perforated ulcers The choice of the method is determined less by the repetitious character of the perforation than by the size, the location and the callosity of the orifice. The authors think that in selecting the method the surgeon should take into account especially the tenacious character of the ulceration, which is the cause of the repeated perforation. They think that in repeated perforation either gastrectomy should be done immediately or a simple method should be chosen which is least likely to interfere with a subsequent gastrectomy.

Postoperative Jejunal Ulcer — The material for this study includes 23 postoperative jejunal ulcers in which operation was performed at the Presbyterian Hospital, New York. Histories of the patients were studied in minute detail from the time of the appearance of the original

duodenal or gastric ulcer, through the operations, and up to the ultimate status at the present time. Nine of the patients did not have their first operation at Presbyterian Hospital.

A. Grossman⁷⁵ presents 10 case reports in detail, each of which demonstrates at least 1 interesting factor in the genesis of postoperative jejunal ulcer. From these data the author has learned that the interval between gastroenterostomy and evidence of the incidence of jejunal ulcer may vary from 12 days to 18 years. In 7 cases more than 5 years elapsed between the operation and the first recurrence of digestive symptoms. In 9 cases the first roentgenological evidence of jejunal ulcer appeared from 6 to 17 years postoperatively. These figures suggest the fallacy of conclusions drawn from gastric surgery based upon a follow-up of 5 or even 10 years.

The material further suggests that the treatment of postoperative jejunal ulcer should begin even before the patient has the initial operation. For example, 6 of the 23 patients were operated upon during their first attack with antecedent symptoms which had been present from 1 week to 3 months. In 9 of the 23 cases, the duration of symptoms was less than 8 months In only 3 cases was there any evidence that medical treatment had been followed faithfully for any appreciable time. Four patients had received practically no medical treatment, although in no case was the operation considered an emergency. In 3 cases (operated upon elsewhere) the records of the symptoms prior to operation were insufficient to permit any conclusions regarding the indication for operation. In no instance in which obstruction was considered the indication for operation had belladonna or any other anti-spasmodic preparation been given a prolonged trial preoperatively.

A long anterior gastroenterostomy is usually followed by a jejunal ulcer, particularly when an enteroenterostomy is added. Three patients developed jejunal ulcers in 6 months, $3\frac{1}{2}$ weeks, and 12 days, respectively. In the cases of these patients, 2 years, $2\frac{1}{2}$ years, 1 year, and 7 years, respectively, had elapsed after the first operation, which in no instance included enteroenterostomy, before the development of jejunal ulcer.

From a study of this material the author concludes that it is obvious that the best treatment of jejunal ulcer is its prevention. This does not necessarily mean the performance of less gastric surgery. The fact that only 23 cases of postoperative jejunal ulcer could be found in the files of the Presbyterian Hospital is in itself a recommendation for gastric surgery. It simply means that absolute indications must be present for surgical intervention and that the patient's unwillingness to adhere to medical measures does not constitute an indication for surgery. The patient should also be properly informed of the importance of dietary measures taken postoperatively He should be warned to return to the most vigorous type of ulcer regimen at the slightest recurrence of symp-Tobacco and alcohol should be forbidden, foci of infection eradicated, preferably preoperatively; and if despite such precautions jejunal ulcer still develops, immediate vigorous medical therapy should be resumed, surgery being reserved for the late complications of jejunal ulcer

Gastrojejunocolic Fistula—Asmany surgeons know, a gastrojejunocolic fistula may be the unfortunate sequence to a gastroenterostomy, performed with or without pylorectomy or other additional surgical procedures, in the treatment of peptic ulcer. The complexity of such a fistula, the fecal contamination of the

stomach and jejunum, the stenosis of the large bowel, and the weakened condition of the patient all are factors which combine to make surgical correction one of the most redoubtable operations in all surgery. Loewy has had occasion to operate upon 5 patients with such a lesion, during the past 5 years.

G. Loewy⁷⁶ believes that, except in rare cases, the surgeon should prepare the patient for 2 separate operations. First, just as soon as there is clinical evidence of the existence of such a fistula. a careful and painstaking dissection of the fistula must be made, with excision of its openings into the stomach, jejunum, and colon, followed by careful closure of these openings Then every supportive care should be given to the patient for at least 4 weeks before the final operation is to be attempted. This consists of partial or subtotal removal of the stomach, with a fresh gastrojejunostomy in a now clean, uncontaminated field, for the cure of the original lesion, the peptic ulcer To repair the fistula and perform the gastrectomy all in 1 stage is courting disaster and it must not be considered unless one's hand is forced.

Loewy uses a combination of spinal anesthesia and sympathetic block. He warns especially against damage to the blood vessels in the dissection of the fistula, and regards this first operation as the one requiring the greatest amount of skill, precision, and methodical treatment. Most patients surviving the repair of the fistula will withstand the subsequent gastrectomy well, and once safely through the first operation they may be expected to attain eventual cure.

Results of Surgical Treatment of Peptic Ulcer—In the year 1916, the surgical department of the Presbyterian Hospital, New York, organized a follow-up clinic for the purpose of recording and studying the results of their surgical

therapy in gastroduodenal ulcerative disease. From the data accumulated in the past 22 years, F. B. St. John, *ct al*, ⁷⁷ reached certain conclusions which they present.

First, they learned that every case must be followed in continuity. In order to do this, graph records were prepared, to enable the examining physician to follow at a glance the course of the case. These charts, which appear in the article, are a most practical, as well as efficient, method of obtaining statistical data on patients with ulcer. In addition, a standard for recording the follow-up results was prepared. The results were evaluated from an anatomical, symptomatic, and economic standpoint. Symptomatic results were the only ones considered in the article.

Four main groups were subdivided as follows Groups 1 and 2 included cases in which the results were unsatisfactory Groups 3 and 4 included cases in which satisfactory results were obtained. Group 3 included the cases of only those patients having no significant symptoms and in whom 'only the mild digestive disturbances to which the normal man is heir" may occur. Group 1 contained those cases in which the results were the least satisfactory of all. If at any time a given case presented unsatisfactory results, it was permanently dropped from the groups with satisfactory results. By a critical appraisal of their follow-up records, it was hoped that it would be possible to establish with reasonable accuracy standards of guidance in the selection of cases for operation, as well as in the choice of operation to be employed for individual cases In addition, the patients were catalogued according to the outstanding preoperative complaints, such as obstruction, bleeding, and pain, with the appreciation that such a separation of cases into these 3 groups could never be wholly accurate

From this study it was found, in the obstruction group alone, that partial gastrectomy gave no better results than gastroenterostomy, and the death rate for the latter was lower. The Finney type of pyloroplasty gave the least desirable results in the cases of patients complaining of obstruction alone.

Seven of the 281 patients studied died of their ulcer at some time after leaving the hospital. In addition, 2 died of pulmonary lesions and 20 died of miscellaneous other causes Partial gastrectomy of the Billroth and Polya types were found most successful for gastric ulcers, as it gave satisfactory results in 92 per cent of the cases. It was found also that the duration of the observation period was most important and that "a distressing number of initial recurrences of symptoms occurred many years after operation" Of the 29 patients who were free from symptoms for 10 years after gastroenterostomy, 5 had recurrences later, i e , before 15 years

An attempt was made to analyze the causes of failure following those operations which were performed most frequently. In a total of 314 individuals, the condition of 118 became unsatisfactory sooner or later, temporarily at least Recurring marginal or jejunal ulcers, demonstrated roentgenologically, peared in about half the patients upon whom unsuccessful gastroenterostomy had been performed, as well as in half of those who had undergone unsuccessful partial gastrectomy. Poorly functioning stomas appeared relatively more frequently among the patients upon whom gastroenterostomy had been performed

An attempt was made to learn how often carcinoma developed in previously benign ulcers, but a conclusion was not reached in this study. Of 88 patients with

gastric ulcer, 3 died of carcinoma, without recognition of the disease at the time the symptoms first developed. The good results that have followed partial resection for benign ulcers have encouraged resection more than ever in the cases of doubtful conditions which do not heal rapidly under medical care. The mortality rate in the cases of 133 patients who had undergone partial gastrectomy was 16.5 per cent. Death from duodenal ulcer occurred in 18.5 per cent of the cases, and from gastric ulcer in 13 per cent of the cases.

Leakage in the suture line was found to have caused somewhere between 37.5 and 68 8 per cent of all deaths. Obstruction was of even greater importance because it was known to have occurred in 9 of 16 fatalities, and may possibly have been present in 5 other cases. Obstruction was believed to be caused by the kinking or twisting occurring close to the site of the anastomosis in either the proximal or distal loop. Four of 6 leaking duodenal stumps were associated with, or probably partly caused by, such obstructions A drain placed in the site of the stump almost as a routine measure should suffice for the leaking duodenal stump. Not one of the surgeons who operated in the 8 cases in which such leakage occurred thought his closure of the stump was insecure, otherwise dramage would have been instituted Inasmuch as it is impossible to predict which stump will yield to the pressure caused by the unexpected obstruction which may or may not be temporary, dramage is recommended. The fistulas which have developed in this series have all closed spontaneously

It was of interest to note that there was little preference between the anterior and posterior Polya technic, from a standpoint of postoperative mortality, or incidence of postoperative complications and follow-up results.

The conclusion is drawn that until the cause of peptic ulcer is known, efforts should be directed, not toward more radical surgery as is the present trend but rather toward selective surgery. This selection can be made only if follow-up results are known and, as surgeons, it is our responsibility to select the patient for the operation and the operation for the patient.

H Finsterer⁷⁸ gives the results in a series of 331 cases in which repeated operations were performed. There was a total mortality of 117 per cent, but 11 dropped to 8.6 per cent if cases complicated by acute perforation, acute hemorrhage, or gastrocolic fistula are omitted The most frequently performed previous operation was gastroenterostomy, 190 cases, after which either the old ulcer had not healed or a gastrojejunal ulcer had formed. The radical operation for a gastrojejunal ulcer, following posterior gastroenterostomy, shows a lower mortality, 68 per cent, than when it follows resection, 235 per cent Therefore, an operation is indicated at once by the return of complaints in a patient after gastroenterostomy, and it is to be delayed if the complaints return after resection until at least several attempts with medical therapy have been made

The mortality rate attending the radical operation for recurrent gastrojejunal ulcer is 21.4 per cent. In acute perforation even the lesser operation, either closure or excision of the ulcer, produces poor results. Radical operation for gastrojejunal ulcer under general anesthesia showed a mortality rate of 42.1 per cent, 19 cases with 8 deaths. Three of these deaths were directly attributable to the anesthetic With local anesthesia the mortality rate was 14.1 per cent. The best permanent results are achieved with the extensive two-thirds to three-fourths re-

section of the stomach and the preparation of the end-to-side anastomosis according to Hofmeister-Finsterer, even though there may have been several preceding operations Of 96 patients, 88 are permanently cured, or 91.6 per cent. The author states that the recurrence of a gastrojejunal ulcer after radical operation is not due to special ulcer disposition but to technical faults, too limited resection. Y-shaped anastomosis or enteroanastomosis. Therefore, by avoiding these errors in technic, permanent cure is possible even after repeated resections The term "surgically incurable ulcer" is not applicable to this type of case. The disadvantages of extensive gastric resection, too small a stomach and anemia are of little consequence since they are more easily controlled than a gastrojejunal ulcer following madequate gastric resection

Partial Gastrectomy for Peptic Ulcer—Comments on the late results of partial gastrectomy for peptic ulcer are made by J. Morley and F. H. Bentley 79. Sixty-seven patients in whom a partial gastrectomy had been performed were re-examined after a period of from 4 to 16 years. The average time of re-examination was 8½ years postoperatively. These 67 patients did not represent a consecutive series, but included only those from a series of 130 patients who could be traced and were willing to return for study.

Fifty-eight of the 67 patients had undergone a Shoemaker's gastrectomy, and 9 had had a Polya gastrectomy Fifty-two patients originally had gastric ulcer, 6 had both gastric and duodenal ulcer, 4 had gastric ulcer and a healed duodenal ulcer, 4 had duodenal ulcer, and 1 had an anastomotic ulcer Thus, most of the patients originally treated had gastric rather than duodenal disease

The group of 9 patients who had undergone a Polya gastrectomy were shown to have depression of gastric function with bile regurgitation and complete absence of free acid. The blood picture showed 5 to have microcytic anemia, and 1 macrocytic anemia. Six of the patients were in good health; 2 were in fair health, although with microcytic anemia, and 1 had been in good health until pernicious anemia developed. There was no postoperative ulceration.

The 58 patients who had undergone a Shoemaker's gastrectomy were divided into 2 groups. Those in Group 1 showed marked depression of gastric function. There was a normal blood picture in 33, and a microcytic anemia in 12; 38 were in good health; 1 had been in good health for 6 years, after which period a gastric carcinoma developed; 6 patients were in fair health, and 4 of these had a microcytic anemia, but only 1 showed symptoms of ulcer.

The patients in Group 2 showed active gastric function, and free acid above 20 cc. N/10 was found to be present. The blood picture was normal in 12, a microcytic anemia, probably secondary to a pulmonary tuberculosis, was found in 1; the general health was good in 10; in 1, the general health had been good for 7 years, after which time a carcinoma developed, and in 2 the general health was fair. One patient in the group with a high free acid value experienced a sense of epigastric uneasiness unless he ate frequently, and 2 had definite postprandial pain

It is interesting to note that a high percentage of anemia was present not only in the patient who had undergone a Polya gastrectomy, and who had depressed gastric function, but in practically all of the patients who had had a Shoemaker gastrectomy and showed depression of gastric function. This sug-

gests that the cause of anemia may be associated with gastric hypofunction The authors conclude that the rôle of hydrochloric acid in this connection has not been entirely proved, and that still another factor—that of rapid gastric emptying-may be of greater significance since it causes incompletely mixed, underdigested food constituents to be hurried through the duodenum and the upper part of the jejunum, and in this way interferes with the absorption of The cause of these microcytic anemias, therefore, may be a diminished absorption of iron, secondary to the depression of gastric acidity. This opinion is substantiated by the observation that considerable improvement is obtained in these postgastrectomy anemias by the administration of massive doses of iron.

However, it was further noted that in patients in whom gastric acidity was not depressed there was a risk of further ulcer development This led to the conclusion that when gastrectomy is performed for gastric ulcer the objective should be to construct a stomach which will prolong the gastric emptying time and lessen regurgitation of the intestinal fluids. It is the opinion that this goal is more readily obtained with the Polya gastrectoniv This conclusion, the authors repeat, applies only to the surgical treatment of gastric ulcer. In duodenal ulcer. where the risk of recurrence is much greater, a more destructive operation has definite advantages

Benign Tumors of the Stomach and Duodenum

Benign tumors of the stomach may belong to various histological types, according to the tissue from which they originate; the commonest are the adenomas and myomas, and the rarest the lipomas and tumors of vascular type. They are sessile or pedunculated, being called polyps in the latter case. Benign tumors of the duodenum occur only rarely as isolated formations, but more frequently as duodenal polyposis associated with gastric and rectal polyposis; they are usually of adenomatous or connective-tissue type and are nearly always found in the first part of the duodenum

The relative frequency of these benign tumors amounts to 69 per 1000 of that of the malignant tumors. The clinical symptomatology is very indefinite, but the roentgenologist usually succeeds in solving various difficulties arising in the interpretation of a gastric tumor by the use of the current technical refinements Generally, the form of the stomach is preserved, its wall appears normal, and active and passive movements are not altered; this also excludes infiltration of the ligaments and mesentery. However, in tumors with intraparietal development. suspicion of a filling defect of cancerous or inflammatory type may arise at first sight, but careful examination will show that the lacuna is well rounded, with distinct borders, similar to that found in compression by extrinsic organs, changes in the position of the patient allow differential study These roentgenological findings apply also to benign tumors of the duodenum, but examination of the first portion of the duodenum is easier than that of the other 2 portions A lacunar defect in the bulb calls for further study, and possible sources of error, such as the presence of foreign bodies and bulbar ulcer with hypertrophic and distinct margins, must be kept in mind

The complications of benigh tumors are hemorrhage, leading gradually to anemia, especially of hyperchromic type with marked hypochlorhydria and even complete achlorhydria; occlusion of the pylorus by a pedunculated tumor; gastroduodenal invagination; and the possibility of malignant degeneration. The

association of malignant and benigh tumors in the stomach has been reported. A purely clinical diagnosis of benigh tumor is nearly impossible, the prognosis must necessarily be reserved, and treatment in case of certain or probable diagnosis must be surgical.

C. Salaris⁸⁰ describes several cases of benign tumor of the stomach and of the duodenum Correct clinical diagnosis was made in 4, while a malignant tumor was believed present in 2, and hemorrhage from duodenal ulcer was diagnosed in 1 The 3 diagnostic errors were due to the impossibility of making the necessary complete investigation of the patients on account of the gravity of their condition on admission. In one of the correctly diagnosed cases, duodenal polyposis had escaped observation because of the preponderance of the gastric symptoms, and was discovered at necropsy. The 4 correctly diagnosed cases included hypertrophic gastritis with polyp formation, gastric polyposis, polyp of the angulus, and polyp of the duodenal bulb. In 2 of the 5 cases of being gastric tumor there was complete gastric achylia with the blood findings of typical permicious anemia demonstrated in the peripheral blood and in the sternal bone marrow, this association can hardly be fortuitous in view of the rarity of beingn gastric tumors and the relative frequency of permeious anemia

Carcinoma of Stomach

The first essential for the development of cancer of the stomach is an intrinsic factor—the constitutional susceptibility to cancer in general. The second essential is a constitutional and inherited organ-inferiority affecting the stomach. However, unless an extrinsic factor in the form of chronic irritation is also present, cancer of the stomach will not develop

Incidence—Cramer has drawn attention to the fact that the total incidence of cancer is approximately the same in all countries, all classes, and both sexes The cancer mortality is, for example, 118 per 100,000 males in England, 120 in Sweden and 118 in Holland This indicates that the first factor—the constitutional susceptibility to cancer—is constant However, the incidence of cancer of the stomach shows remarkable differences in different nations and classes stomach accounts for only 22 per cent of the deaths from cancer in males in England compared with 45 per cent in Sweden and 55 per cert in Holland, and cancer of the stomach is twice as frequent in the lower social classes in England as in the well-to-do, whereas the incidence for the colon and rectum is the same variations of the incidence in different social classes and in different countries involve both ulcer-cancer and gastritiscancer. It is therefore likely to be due to extrinsic factors and not to any constitutional difference in the resistance of the stomach to disease, a difference which would in any case be extremely unlikely to exist

Sir \ Hurst\1 points out that though the total incidence of cancer is the same in males and females, in England in 1935 the stomach was affected in only 166 per cent of the temales with cancer, compared with 22.5 per cent of the males who developed cancer. The fact that the total incidence of cancer is the same in both sexes appears to be due to the deaths from cancer of the breast and uterus in women who would otherwise have developed cancer of the stomach This does not mean that there is any difference in the liability of the stomach to become malignant. Carcinoma of the cervix, which accounts for 90 per cent of cases of uterine cancer, and carcinoma of the breast occur 20 and 15 years

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respectively, earlier on an average than carcinoma of the stomach. Consequently, if a woman who is predisposed to cancer is subjected to the predisposing and exciting causes of both cervical or breast carcinoma and gastric carcinoma, she is likely to develop one of the former at a period when gastric irritation has not been operative for a sufficient length of time for cancer to develop in the stomach.

Cancer of the stomach is commonest between the ages of 55 and 65; but, when allowance is made for the number of people living at each age, it is found that there is a steady rise in the incidence throughout adult life. This is not due to increasing susceptibility as age advances but to the fact that the exciting causes act very slowly.

Achlorhydria is present in about 65 per cent of patients with cancer of the stomach or more than 4 times as frequently as in the general population, and an extreme degree of hypochlorhydria is present in an additional 5 per cent. In 15 per cent there is good evidence that the growth is secondary to a chronic ulcer. This leaves an indeterminate 15 per cent, of which perhaps 5 per cent reveal that the cancer developed from the malignant degeneration of a simple adenoma, and the remainder can probably be equally divided among the gastritis-cancer and ulcer-cancer cases, the former being cases in which the initial acidity was comparatively high and the free acid had not disappeared in spite of the presence of gastritis. It was formerly believed that the achlorhydria present in about 65 per cent of the patients with caremona of the stomach was a result of the carcinoma, but in 1929 the author brought forward evidence to show that the achlorhydria is caused by chronic gastritis, which is present before the growth develops as a result of malignant degeneration of the inflamed mucous membrane

The occasional association of carcinoma of the stomach with pernicious anemia has long been recognized. Now that most patients with pernicious anemia can be kept free from recurrence indefinitely with liver extract, an increasing number is likely to develop carcinoma of the stomach

Although the type of gastritis which predisposes to cancer appears to affect the whole or the greater part of the stomach more or less uniformly, and although a very large majority of chronic ulcers is situated on the lesser curvature of the stomach and in the duodenal bulls, cancer is more common in the pyloric region than anywhere else in the stomach and never involves the duodenal bulb. The additional factor predisposing to the development of cancer in the pyloric region is probably friction. No churning occurs either in the fundus or in the duodenal bulb.

Alcohol appears to be of less importance as a cause of precancerous gastritis than of precancerous esophagitis, for in the alcohol trades the incidence of gastric cancer is less than double that of the general population compared with the incidence of cancer of the esophagus, which is 4 times that of the general population

Class differences in the incidence of cancer of the stomach must be due to defective alimentary hygiene among the poor, the most important factors probably being septic teeth and lack of an adequate number of teeth for efficient mastication. Other likely factors are coarse and less well cooked food and stronger tobacco.

One means of improving the prospects of a permanent cure after a successful gastrectomy would be for surgeons to recognize that a local recurrence is more

often due to a continuation in the remaining portion of the stomach of the process which led to the development of the primary growth than to failure of removal of the whole of the tissue already invaded by cancer. That is to say, the residual gastritis requires most careful treatment by diet and the removal of all sources of irritation after the operation in order to prevent further malignant degeneration.

Whereas carcinoma is no commoner in the stomach and colon of males than of females if allowance be made for the frequency of cancer of the breast and uterus in women, this is not the case in the middle and lower end of the esophagus, where cancer is rarely found in women This can be due only to a sexual difference in the extrinsic causes, the most important of which are probably tobacco and alcohol, which must exert a much more concentrated action on the mucous membrane of the esophagus than on that of the stomach, for the former is always empty, whereas the irritant is diluted by the food and gastric juice found in the stomach

Whereas the meidence of cancer of the stomach in the very poor is over double that in the well-to-do, the incidence of carcinoma of the colon, including the rectum, is approximately the same in all classes. It is considerably higher in men than in women, but if cancer of the breast and uterus be excluded, no appreciable difference remains

F Christopher⁸² shows that gastric carcinoma is still the "unsolved problem" The subject is worthy of repeated examination and study because of its frequent occurrence and its curability in the early stages. Earlier diagnosis and improved surgical treatment will go far to lower the death rate and to diminish the suffering caused by this disease. The public and even a large part of the med-

TABLE 6 CANCER MORTALITY IN THE UNITED STATES, 1936

(U. S. Public Health Reports)

Total deaths from cancer 142,613 Cancer of stomach and duodenum (practically all stomach; 19 per cent of total deaths) (male, 16,210, female,
11,031) 27,241
Cancer of the uterus 16,280
Cancer of the intestines (except duode-
num, rectum, and anus, nearly all
large bowel) 15,364
Cancer of the breast 13,708
Cancer of the liver and bile passages . 10,425
Cancer of the rectum and anus 7,325
Cancer of the prostate 7,140
(Other organs in diminishing frequency)
(Estimated annual death rate from carcinoma
of the stomach, 38,000)
(Mortality, carcinoma of stomach, 21.1 per
100,000 population, on basis of 27,000 an-
nual deaths)

ical profession are unaware of the great help that surgery can give to the people suffering from this disease

Cancer is second among diseases as the cause of death, and in 1936 the rate was 111 per 100,000 population. The leading importance of cancer of the stomach as a cause of death may be seen from the above table

The estimates of various authors as to the annual mortality from cancer of the stomach in the United States are somewhat at variance with the statistics of the Bureau of Census Horsley estimates 35,000 and Collins 38,000 Pack believes that 35 per cent of all deaths from cancer are due to gastric carcinoma Morley states that the 1934 mortality from cancer of the stomach in England and Wales was 12,269 Burgess believes that gastric cancer causes about one-third of all the deaths from cancer in England. Cancer in general is said to be commoner in the poorer classes

(Stout), and curiously enough its death rate is 3 times as common in Massachusetts as in Arkansas.

Diagnosis - The early diagnosis is difficult, but should be made much more frequently In very early cases, surgical treatment should cure the great majority of cases. "Indigestion" or loss of appetite should be regarded seriously in any patients over 30 years. The symptoms may suggest those of ulcer or even of cholelithiasis. The roentgen examination is the cornerstone of the diagnosis and should be made upon the slightest suspicion and repeatedly. "Limp" in peristalsis and changes in mucosal patterns often will give a clue to early diagnosis. The late roentgen diagnosis is usually easy. The present operability of carcinoma of the stomach is only about 20 per cent and should be greatly increased. The operative mortality of gastric resection in skilled hands should be less than 15 per cent In Balfour's large series of cases 48 per cent of the patients having gastric resection for carcinoma when there were no metastases lived 5 years Thirty per cent of those with and those without metastases grouped together lived 5 years. Twenty-three per cent of Warwick's patients with carcinoma of the stomach died without metastases The best palliative operations are gastric resection and exclusion (Devine) Painless death from liver metastases seems preferable to starvation from gastric obstruction. Age and the general condition of the patient are usually inconclusive so far as the prognosis goes, and x-rays are unreliable in the determination of operability. Survival after gastric resection for caremoma for as long as 24 vears has been reported and 10-year survivals are not uncommon

Perforation in Gastric Carcinoma— The opinion seems to prevail that perforations in carcinomatous stomachs are rare Two cases of frank perforation within a few months prompted R. W. McNealy and R. F. Hedin⁸³ to make a study of all cases of carcinoma of the stomach which had been admitted to Cook County Hospital and Wesley Memorial Hospital during the 12 years (1925-1937). Of 3289 cases of gastric carcinoma, there were 133 perforations (404 per cent).

Types—The group of perforations is divided clinically into the "classical" and "obscure" types. The classical type includes those cases which clinically appeared to be perforations into the general peritoneal cavity. The obscure type includes those cases in which there was localization of an abscess or a sealing off of the perforation. Both types are quite evenly represented in the series of cases.

Diagnosis—The condition was correctly diagnosed in 31.6 per cent of the cases. Free air in the peritoneal cavity as shown by fluoroscopic examination was found to be a valuable diagnostic procedure

A study of the incidence of the various symptoms and findings is presented. It is stressed that after perforation has occurred, examination of the abdomen is quite difficult and that a careful history must be relied upon in making the diagnosis.

As shown by the authors' series of cases, cancer of the stomach may perforate irrespective of the location of the lesion. However, the lesser curvature, prepyloric region, and cardiac end are the commonest sites.

Pathology—Of 71 cases submitted to pathological examination, adenocarcinoma, ulcerative adenocarcinoma, and ulcerative carcinoma accounted for 50 perforations.

In 53 cases, including 17 which were not proved to be perforations but which had quite typical chinical findings, the

perforations occurred into the general peritoneal cavity. Perigastric abscesses, gastrocolic fistulas, and subdiaphragmatic abscesses were also common sequelae of obscure perforations.

Prognosis—Various surgical difficulties were found in the 63 patients operated on, and various types of operations were done. In 70 patients no surgery was attempted, either because a diagnosis could not be made or the condition of the patient did not warrant surgical intervention. The immediate operative mortality rate was 58.7 per cent. Only 13 patients left the hospital as improved.

Treatment—The surgical treatment in perforation of carcinoma of the stomach should be to aim at radical removal of the carcinoma. Simple closure of the perforation with or without a gastroenterostomy to relieve any obstruction is usually the only procedure attempted immediately following the perforation. More formidable procedures, such as partial resection of the stomach, must often be reserved for a later date when the patient is in better condition to stand extensive surgery.

It is the authors' opinion that if a biopsy of all perforations thought to be due to beingn peptic ulcers were done, many would be found to be malignant. If this routine were carried out, many patients might have the benefit of early resection

Preoperative Preparation of the Cancerous Stomach – Peritonitis was the cause of death in 72 per cent of the 132 fatalities following the operation for gastric cancer in the experience of S. A. Abramovich 84. The author comments on the method of Friedrich, of administering dilute hydrochloric acid and washing the stomach of patients about to be operated on for gastric cancer with 0.25 per cent hydrochloric acid. The report is given on a bacteriologic study under-

taken to determine the effect of this treatment on bacterial flora of the gastric Sixty-four patients with gascontents tric achiylia about to be operated on for gastric tumor were given a tablespoonful of diluted hydrochloric acid in a glass of cooled boiled water 3 times daily. Their stomachs were washed daily with large quantities of cooled boiled water. followed by from 0.5 to 1 liter of 0.25 per cent solution of hydrochloric acid. These studies demonstrated that the anacid gastric contents of gastric cancer patients are never sterile The oral administration of diluted hydrochloric acid in the course of several days before the operation destroyed certain types of microorganisms and diminished the number of colonies of other types Drinking of the solution combined with the lavage accelerated the cleansing process maximum bactericidal effect was accomplished in from 30 to 60 minutes, after which period the bacteria increased in numbers. The author suggests, therefore, that hydrochloric acid lavage be practiced immediately before the operation. While the author realizes that the primary factor in the reduction of the postoperative mortality is the proper choice of operation and adequate technic, he believes that partial reduction of pathogenic microorganisms of the gastric contents may be regarded as an additional factor in reducing the postoperative peritonitis

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APPENDICITIS

By Frederick A Fiske, M D

Etiology—Following studies which proved that the appendix secretes fluid, Wangensteen and C Dennis¹ carried their experiments further by obstructing the appendix in man The appendix with its blood supply intact was exteriorized through a buttonhole incision, and was obstructed at its base Studies were made on 22 patients determining by manometric readings, the maximum pressure in the appendix, the time required to reach this pressure, the duration of time maximal pressure was sustained, the total fluid after end of recording, the period of fluid collection, the lapse of time between onset of experiment and removal of the appendix, and histological studies at the onset and end of experiment

From these experiments it was concluded that the secretory pressure in an obstructed appendix may approach the systolic blood pressure. The histologic picture of acute diffuse appendicitis has been produced in man by obstructing the exteriorized appendix. An appendix with an attrophic mucosa failed to secrete fluid when obstructed. It appears likely that the chief inciting agent in bringing about appendicitis in man is obstruction of an appendix in which the mucosa possesses the normal secretory capacity.

In contrast with the usual fecaliths as a cause of obstruction of the appendix, Bunch and Adcock² report the rare finding of a true calculus of the appendix. In their case the appendix contained a giant calculus in the sacculated distal end with 4 smaller calculi near the base. All 5 were faceted, the wall of the appendix around the large stone, which weighed 13.5 Gm, was thin with an absent muscular layer. They feel

that attacks of catarrhal inflammation leads to repeated outpouring of mucus into the lumen of the appendix with the deposition of inorganic salts due to stasis. As the stone enlarges it excites inflammation with more secretion and deposit of inorganic salts, thus a vicious cycle is established. Should complete obstruction occur a retention cyst or mucocele may develop, eventually leading to pseudomyxoma.

In a study of the etiological factors in 3400 consecutive unselected cases of acute appendicitis, Collins³ demonstrated that fecaliths and concretions in the lumen were the commonest factor (30.23) per cent) of severe acite appendicitis, and that by hypertrophy of the lymph follicles, stenosis, and kinks produced the obstruction in 20.64 per cent. The other factors were enterogenous origin, 1045, hematogenous origin, 1.35, foreign bodies in the lumen, 145; parasites in the lumen, 0.79 per cent, and cause unknown, 3481 per cent Obstruction of the appendiceal lumen was responsible for 81.22 per cent of the examples of acute gangrenous appendicitis, while the same factor caused 79.63 per cent of the instances of perforative gangrenous appendicitis

The rôle of heredity as an etiologic factor in appendicitis has been reviewed by Perry and Keeler ⁴ They have studied a pedigree containing 39 individuals who have suffered from appendicitis. The tendency to appendicitis is hereditary in this pedigree, and seems to involve the transmission of several different types of predisposition. They conclude from this study and a review of the literature that there are many factors predisposing to appendicitis (some of which fac-

tors are inherited as irregular dominants), and that the genes for several of these predisposing physical factors are concentrated in the germ plasm.

According to Grettve⁵ the significance of trauma as an etiological factor in post-traumatic disturbances of the appendix has been overemphasized. If blunt force hits the lower right abdomen, directly and violently, it may in rare cases result in real damage to the appendix Trauma may cause a flare-up of old pathological lesions of the appendix, and it is difficult to appraise the rôle which trauma has played in influencing the final outcome of the disease.

Pathology—After histologic study of the mesenteriola of 245 appendices in various stages of the disease, Beluffi⁶ concluded, that every inflammatory process of the vermiform process is accompanied by demonstrable lesions in the mesenteriolum. The lesions vary from case to case according to the type of appendicitis. In general the severity of these lesions is proportional to the intensity of the anatomic pathological process occurring in the wall of the appendix. Following an attack of appendicitis certain structural changes persist in the mesoappendix which will permit a retrospective diagnosis of previous appendicitis

In the acute phase of appendicitis, the reactions in the mesenteriolum include edema, exudation, infiltration, lymphangitis, rapid mobilization of the reticulo-endothelial elements, and pervascular infiltrations. In more severe cases there is an impairment of the circulation and a thrombosis of the venous radicles which may lead to a purulent mesenteric thrombophlebitis and a hepatic abscess. After subsidence histological changes in the form of thickening of the connective tissue, blood-vessel walls and follicular

infiltrates are observed. Microscopically these old lesions appear in the form of shortening adhesions and retractions which tend to alter permanently the anatomical relationships and physiological properties. These cicatricial changes in the mesentery produce various mechanical and functional disturbances in the appendix which favor stasis and predispose to future attacks.

Morphologic deviations of the 2 muscular layers, with attenuation or thickening, disappearance and the production of supplementary fibers have been observed by Goldner 7 Aberrant fibers appear ectopically, forming median coats, surrounding lymph follicles or lying in the fibrous capsule of the submucosa. These changes are frequently seen in chronic and subacute appendicitis and rarely in acute and normal appendices They denote past attacks and exist even when other cardinal signs have subsided Functional changes in the form of abnormal contraction should correspond to these structural abnormalities. This may be as important etiologically as changes in the connective tissue framework. Although the majority of aberrant muscular structures appear permanent, others may fall prey to sarcolysis or rearrangement

Bizard, Driessens and Malatrav⁸ summarized 21 cases of sarcoma of the appendix from the literature, and report a case of their own. The patient was a male, 27, with a large tumor in the right iliac fossae which had rapidly grown in the past 11 months. The tumor had never caused pain or symptoms other than slight constipation and some dysuria Clinical and roentgenological examinations showed it did not involve the intestines, but apparently arose in the mesentery. It was removed at operation and pathological examination showed it to be a lymphoblastic sarcoma was no recurrence 3 years later

22 cases reported lymphoblastic type was observed in 72 per cent; fibroblastic type in 13 per cent. The tumor was noticed by the patient in 90 per cent of the cases. Pain was generally associated There were often some digestive disturbances, and in some cases a rapid loss of weight.

In the small series of sarcoma of the appendix reported, there were 2 found at autopsy; no follow-up in 5 cases. In 50 per cent of the remaining cases, operation gave good results without recurrence for from 1 to 4 years. One patient died a few hours after operation; 3 died in less than a year of unknown causes, 2 had recurrences in 4 and 8 months, 2 died of metastases.

Symptoms — Classical symptoms of appendicitis are not always present. Demmer⁹ found 14 per cent of 1400 cases were atypical According to his observations over a period of 15 years, the difference between axillary and rectal temperature in acute inflammatory disease of the abdomen has been an aid in diagnosis. Normally the difference amounts to 05° C, with intra-abdommal inflammation this difference increases in a few hours. The difference has not been observed in inflammatory conditions of the chest. Although the temperatures may be within normal limits the difference between the 2 is the significant feature

Differences of 1° (are an indication for urgent surgical intervention, while 0.6° to 0.7° (are regarded with suspicion. When other symptoms are lacking, temperatures are taken every 3 hours, if the difference is increasing the condition is probably progressing. This difference may be noted in cholecystitis, inflammatory or perforated gastroduodenal ulcer, or pelvic inflammatory disease as well as appendicitis. In the presence of positive clinical signs the

temperature difference is lacking in only 0.05 to 0.06 per cent of the cases. He was misled by positive temperature difference in only 1.5 per cent, in which a febrile or grippelike condition of the intestines was present.

He classified the diagnostically difficult cases into (1) The ambulant patient with atypical and indefinite symptoms. (2) The patient with acute gastroenteritis associated with appendicitis. (3) Paralytic ileus with or without appendicitis. (4) The combination of cholecystitis, inflamed ulcer of the stomach or duodenum, or pelvic inflammatory disease with appendicitis (5) Patients with appendicitis who believe that the appendix was removed at previous operation Instructive histories to illustrate the diagnostic sign are cited.

Discussing the referred and localized types of pain in relation to extra-abdommal diseases simulating the acute obdomen, Kilgore¹⁰ points out that careful attention may distinguish differences between these types of pain. True visceral pain is produced by tension (1) within a hollow organ distended with fluids (2) within a smooth muscle tube in spasm over a stone or (3) in tissue swollen by inflammation -The referred pain is superficial and accompanied by tenderness of the skin to pinching, scratching or pricking. The tenderness of visceral disease is demonstrated on slow, steady deep pressure over the abdomen

The similarity in the symptomatology of acute appendicitis and acute mesenteric lymphadenitis, has been pointed out by Foster ¹¹ The main difference between the 2 conditions arise from the anatomical location. In the mesenteric lymphadenitis (1) there usually is a history of an acute upper respiratory infection 1 to 2 weeks preceding the attack, (2) the attack is often initiated by the onset of pain which appears more dull

and continuous than the colicky type seen in appendicitis; (3) it is common in children and young adults who are undernourished; (4) there is sometimes generalized lymphadenitis; (5) it is common to see objective evidence of infection of upper respiratory or oral tract; (6) tenderness usually is present around umbilicus and right or left lower abdominal glands may be palpable; spasm and rigidity are variable; (1) constipation is present with doughy descending colon; (8) distention is not uncommon, less frequently associated with spasm and rigidity; (9) variable evidence of the existence of more than 1 intra-abdominal disease appears to favor the diagnosis of mesenteric lymphadenitis. It is pointed out that either diagnosis requires a laparotomy.

Quinckes' edema or visceral urticaria may be mistaken for acute appendicitis as shown by the case reported by Redon 12. The patient was subject to frequent urticarial crises, especially after fish. Before his attack he had eaten fish and mussels. At operation a sparkling edematous mass in the ileocecal region was found, and a normal appendix was removed

Roentgenologic Examination-By roentgenological observations covering a period of 7 years, Sahyoun and Oppenhermer¹³ have been able to determine that an appendix is healthy when it fills within 6 hours after the beginning of gastric evacuation, empties before the cecum does, is uniform in caliber, and is dense and homogeneous in contrast Free mobility and absence of tenderness are not essential Stasis in the appendix indicates a disorder of the intrinsic appendicular activity In appendicitis, whether acute or chronic, stasis in the appendix is the leading roentgen sign The barium is retained in the appendix after evacuation of the entire colon or the

cecum at least. Even in those acute cases in which swelling of the mucosa causes scanty and delayed filling, stasis is always associated It was observed that whenever stasis was found roentgenologically, certain histopathological signs of chronic inflammation were demonstrable in the muscularis of the appendix, especially with lymphocytic infiltration and degenerative changes in the ganglion cells of the plexus of Auerbach and Meissner. The foci of lymphocytes were scattered throughout the muscularis, at times also in the serosa, in practically all the cases acute appendicitis. Inflammatory edema, indicative of acute inflammatory swelling of the appendicular mucosa, may be recognized roentgenologically by circumscribed rounded prominences bulging into the lumen of the appendix.

The reflex actions of the stomach and colon upon the appendix, were studied by Fieschi and Zelaschi. The stomach and colon were distended by air. The observations may be summarized by the statement that a filled stomach produces reflexly hypertonic and hyperkinetic reactions in the appendix. The reactions stimulated by distention of the colon were chiefly hypertonic. In both cases the reactions to stimulation were markedly altered or absent in the pathologically affected apendices

Acute Appendicitis — A series of 1010 consecutive cases of acute appendicitis was analyzed by Hawk and Woodhouse ¹⁵ They were grouped into Nonperforated, 821, acute, 670 (66 33 per cent), gangrenous 151 (1495 per cent), and perforated, 189; abscessed, 68 (678 per cent), local peritonitis, 111 (1095 per cent), diffuse peritonitis, 10 (099 per cent) There were 21 deaths, including nonoperated as well as operated cases, giving a group mortality of 208 per cent, 18 of the deaths were in the 189 perforated cases, giving a mor-

tality for this group of 9.52 per cent. The mortality in the 10 cases which had general peritonitis on admission was 60 per cent It was found that acute appendicitis was most frequent between 16 and 20 years of age, and that gangrene and perforation were proportionately higher in the ages before 6 and after 50 years The male is afflicted more than the female (529 to 481) and is more likely to have the infection go on to a complication than the female A seasonal increase of 15 per cent was noticed in the spring and summer, over the fall and winter. Laxatives and delay in seeking surgical aid predisposed to the complications of acute appendicitis

They attribute the favorable mortality to early emergency treatment of all cases of acute appendicitis with conservative treatment of localizing abscesses and certain very ill late cases of perforation with local or diffuse peritoritis use of the McBurney incision was beheved to be of value in lowering the mortality, because of the accessibility of the appendix, and diminished trauma to the bowel and the unlikelihood of spreading infection when perforation has already occurred. The use of dramage material is decreasing, although it is still used in many cases of perforation and abscess. It is infrequently used in the gangrenous nonperforated cases even when cloudy fluid is present. Enterostomy is still useful in badly distended patients who do not respond to Wangensteen deflation. An appeal is made for a "break-down," analysis of the cases of acute appendicitis reported, so that something may be learned from them

Chronic Appendicitis—A review of 8 different lesions of the appendix which are clinically called chronic appendicitis was made by B J McCloskey ¹⁶ The lesions are chronic appendicitis (pathologic), fibrous stricture, chronic oblit-

erative appendicitis, adhesions, peritoneal bands and membranes (congenital). kinks, fecaliths and fecal column, foreign bodies These lesions may produce definite clinical symptoms over a period of time and prepare a pathologic background for a severe acute attack. It is necessary for the surgeon and the pathologist to co-operate in the study of these cases. It was felt that these conditions deserve important consideration in our campaign against the rising mortality and morbidity of acute appendicitis. The importance of recognizing these lesions as a cause of abdominal pain by the medical practitioner is emphasized

Roentgenological studies were made in 142 cases of chronic appendicitis in which operative intervention was resorted to by Plisan and Gringauz 17 The appendix was visualized in 67 per cent They consider x-ray studies a valuable method of making a diagnosis of chronic appendicitis Persistent irregular filling observed on repeated examination suggests a pathologic state. Failure to fill is also a valuable sign. Strictly localized tenderness of the appendix combined with loss of its motor function and limitation of motion when combined with the foregoing signs is pathognomonic of chronic appendicitis

Technic of Operation-The question of invagination of the stump of the appendix or noninvagination is unsettled. Many surgeons follow each technic with logical reasons for their method. Donaldson and Thatcher¹⁸ investigated 3 groups of animals in which the appendix stump was ligated and not invaginated, and invaginated with silk and catgut purse string sutures. They found adhesion formation was greatest when the stumps were not invaginated, less when a catgut purse string was used, and least when a purse string suture of untreated black silk was used. The pos-

sibility that the catgut purse string may, in the human, be more likely to predispose to abscess and fistula formation than occurs with the noninvagination technic was considered Donaldson, who had previously used the noninvagination technic for 8 years, has returned to the use of silk purse string as a result of his experiments.

Experimental studies regarding the tissue reaction produced in the peritoneal cavities of dogs by: department store silk equivalent to size 1, sizes 1 and 2 specially treated waxed surgical silk; chromic 0 and 00 nonboilable 20-day silk untreated, were conducted by Donaldson and Cameron.19 It was found that less adhesions occurred with department store silk or untreated silk than any other material tested, and the most extensive adhesions were produced by From the experiments it waxed silk was felt that continuous sutures of silk were safe. It was found that untreated silk is slowly absorbed in the tissues They recommend clinical application of the Noble plication procedure when it is necessary to cover rare surfaces of the bowel

Sylvestre²⁰ reports a case which illustrates the danger of invagination of the appendiceal stump with linen suture. The patient had a tumor of the right iliac region with slight pain, colic and fever, which was shown by operation to be an inflammatory tumor, in the center of which was a loose ligature of linen. He believes that linen thread possesses clinical and physical factors which excite an inflammatory reaction without infection, the purpose being to expel the linen thread.

The relationship of the McBurney type of incision, or some modification of it to mortality and morbidity in acute appendicitis has been emphasized by many

It seems sufficiently proven to warrant further emphasis under operative technic

Treatment—The greatest controversy in the management of appendicitis occurs in those late cases where perforation, and peritonitis have already occurred when the case is seen by the surgeon. It is also in these cases where the greatest mortality is encountered. Between the conservative treatment advocated by Ochsner and the radical immediate appendectomy regardless of the stage there is a wide difference of opinion

In an editorial, Ochsner²¹ has emphasized that there is no conservative treatment for appendicitis, operation should always be done. It is in the cases of late perforation with peritonitis where the conservative treatment is of value. in these cases additional operative trauma may produce a fatal result. It has been reported that one of the disadvantages of conservative treatment is the complications which occur To this he answers that patients live long enough to develop complications, i e, pelvic, subphrenic, and other residual abscesses recognition and the institution of adequate drainage, however, will result in cure He emphasized the fact that conservative treatment is more difficult and taxes the judgment of even the experienced surgeon. He is convinced that the physician who sees relatively few cases will do better by operating immediately on all cases, irrespective of the time and presence or absence of complications

According to Shipley 22 the knowledge of when to operate, and when and how to drain, constitutes the most important problem in peritonitis complicating acute appendicitis. In a study of 1106 cases of acute appendicitis, peritonitis which is not accompanied by gross perforation was considered early and the gross contamination which occurs after rupture

is called late peritonitis. Patients with early peritonitis were treated by immediate appendectomy with drainage of the abdominal wall after closure of the peritoneum. Also included in this group were a number of patients in whom rupture of the appendix had sealed off The late peritonitis may be localized, diffuse or subsiding. The localized peritonitis may be so from its onset or it may occur as a result of conservative treatment of a diffuse peritonitis. As soon as localization occurs it is believed that the abdomen should be opened and drained, without attempting to remove the appendix. It was felt that conservative type of therapy was the best in the diffuse peritonitis group. The McBurney incision was advised. Drainage material should be soft. The danger of pressure necrosis from hard drains was emphasized

Radical Surgery—In a series of 972 cases, which constituted every case of acute appendicitis or peritonitis from appendicitis, treated by Horsley and sons^{23, 24} there were 6 deaths, a mortality rate of 0.617 per cent. The cause of death was: (1) A woman, 34, had an appendectomy, and an abscess of the left tube and ovary which involved the ileum Resection of the ileum was followed by intestinal obstruction and death in 5 days. The prime cause of death was not appendicitis, but the case was included since the appendix showed acute inflammation (2) A white male, 84, who had a high appendix under the liver removed under local anesthesia. Death followed 14 days after the operation. Necropsy showed a gangrenous gall-bladder This was a case of mistaken diagnosis, which may have been omitted from the statis-(3) Male, 59, pulmonary embolus sixteenth postoperative day. (4) Male, 50, death on sixth day of uremia, cirrhosis of liver and acute nephritis proven at autopsy. (5) Male, 72, died on fifth

day of pulmonary edema and paralytic ileus. (6) A girl aged 17 years who had a ruptured appendix, spreading peritonitis, and gangrene of 3 feet of intestine. The appendix was removed and intestine resected. She died of overwhelming infection 8 days later. Excluding the first 2 cases of a mortality rate of 0.41 per cent was obtained.

In summary they stated that every patient was operated on as soon as the diagnosis was made, and the appendix was removed in every case. They feel that the morbidity and mortality as well as the financial burden are lessened by this treatment. The immediate operation and removal of the appendix must depend upon other points, on suction, intestinal rest, gentle handling of the tissues, simple treatment of the stump, and McBurney incision These commendable results challenge others to duplicate them

Williamson and Rankin²⁵ report 32 consecutive cases of appendicitis which had gone on to perforation with general peritonitis without a death. They advise immediate removal of the appendix, after a brief period of preoperative preparation. The incision used was a median or lateral right rectus All cases were drained with 1 to 3 Penrose cigarette drains, which were removed on the second or third day. The peritoneum was closed down to the drains, the fascia and skin packed open with gauze saturated with tincture of merthiolate, azochloramide or similar antiseptic. through and through sutures were placed but left loose, in order to approximate the wound as infection disappeared. The treatment of the stump was not mentioned Ventral drainage by placing the patient on his abdomen and elevating the head of the bed 8 to 12 inches was immediately instituted Prostigmin, 1 ampoule every 4 hours, was used. It

was observed that profuse drainage occurred during the first 24 hours. The average hospital stay was 20.9 days. No incisional hernia was noted.

Serum—The management of 98 patients in whom spreading peritonitis developed as a complication of acute perforated appendicitis is discussed by Bower, et al.26 One or more laxatives were given in 90 per cent of their cases. They feel that laxative-induced peritonitis is more virulent than spreading peritonitis not so induced. Perfringens antitoxin (20 cc -10,000 units each of perfringens and vibrion septique) was used on 46 patients. In none of these did delirium develop before operation; however, it occurred in 1 patient postoperatively who had a urea nitrogen of 50. Of 52 patients who were operated upon and then given the antitoxin, mental irritability and delirium were not uncommon. The mortality was 652 per cent for the 46 patients and 15.39 per cent for the 52 patients. Continuous intravenous injection of 10 per cent dextrose was used to keep the patients in metabolic balance as well as fluid and immunologic balance.

Drainage — According to Warren²⁷ primary closure of the peritoneum in perforated appendicitis without abscess 15 a safe procedure and warrants further trial in an effort to lower the high mortality rate In a review of clinical evidence he cites the work of Hotchkiss, Bauer, Wildegans, Clairmont and Meyer, Hall, Shipley and Bailey, Marchini, Carfritz, Kulenkampff and Muelleder, Colt and Morrison and Giertz in support of nondrainage of the peritoneum experimental work of Yates, Rost and others indicate that drainage of the peritoneum is of doubtful value A comparative study was made of 111 cases of appendicitis in which one of these criteria was satisfied: (1) Free organisms

in the peritoneal cavity at operation, proven by culture; (2) an open perforation described by the operator or (3) an open perforation described by the pathology department. Of these cases, 91 were drained and 20 were not drained, and the statistical results are seen in Table 1. The impressions were favorable, the patients were not as sick, the complications and mortality seemed to be reduced in the undrained cases.

Of 172 cases of perforated appendicitis Clairmont²⁸ found a generalized exudate in 146 cases; of these 86 were infected, 26 sterile, and 34 not examined. The total mortality was 4 per cent. Eighty-six per cent were closed without drainage. Independent of this series was a group of 81 cases of most serious diffuse peritonitis with a mortality of 37 per cent. In the undrained cases the mortality was 28.5 and in those widely drained 57 per cent. He feels that the postoperative treatment in undrained cases is very important and sometimes surgical intervention for abscess is necessary.

The possible abscesses are. (1) Anterior parietal abscess easy to diagnose and open. (2) The mesoceliac abscess, deep in the ileocecal region, more difficult to diagnose but easy to open. (3) Right ileo-inguinal abscess, easy to diagnose (4) Abscess in pouch of Douglas diagnosed by digital examination, aspirating needle and drainage through the rectum. (5) Suprapubic abscess with bladder symptoms, easily felt in the midline above the symphysis. (6) Abscess on the left side which is an absolutely regular type found in children. It appears 2 fingers above the left inguinal ligament to the medial side of the colon and is easy to recognize and drain. (7) Left subserous inguinal abscess, external and anterior to the colon. Opening is made as far lateral as possible to avoid free peritoneal cavity. (8) Left subphre-

TABLE I											
Comparative	STATISTICAL	STUDY	OF	111	CASES	OF	PERFORATED	APPENDICITIS,	WITH	AND	
WITHOUT DRAINAGE											

	Mort	ALITY		Incidence of	Fecal	Wound	Postopelative Reactions			
	Due to Due to		Totals	Secondary Abscess	Fistual	Infection	Average	Average	Average	
	Casas	Pe ito-		Re i'il ing Drainage	Total Incidence	Total Incidence	Maximum Temperature	Days Before Temperature Normal	Days Before First Powel Movem int	
Undrained Localized										
abscess, 3 cases	0	0	0 In 15 cases*	0	0	190%	In 3 cas's 101 6°F	In 3 cases 14 2 days	In 3 cas s 50 days	
Diffuse, 17 cases	3, or 17 6%	1, or 5 8%	9, or 6	3, or 2 0~	0	136%	In 17 cases 103 0°F	In 17 cases 15 2 days	In 17 cas's 47 d vs	
Crained Localized abs ess, 31 cases	2, or 6 4%	2, or 6 4%	0	0		10 °′ _c	In 30 cases 102 1°F	In 24 cases 11 7 days	In 3 cas s 5 2 days	
Cifus", 60 cases	11, or 18 3%	9, or 15 0°%	In 57 cases 10, et 17.5%	5, or 8 7%	In 83 cas 's 4, cr	1')0' (In 48 cases	In 50 cases 4 4 days	

^{*}Hereafter, the number of cases analyzable is somewhat d minished through d letting these which died too early for consideration (Warren Ann Surg.)

mc (9) Abscess in middle of peritoncal cavity is infrequent and is difficult to diagnose and treat (10) Right retrocecal abscess is very frequent in acute retrocecal appendicitis but seldom occurs during the postoperative course Right subserous inguinal abscess. This is situated lumbar to the surface of the ascending colon (12) Right subphrenic abscess, which may occur either antenorly but usually posteriorly. The diagnosis may be difficult and extrapleural dramage is best (13 and 14) Abscess in the mesentery of the small intestine or beneath the hepatic flexure of the colon is rare, both difficult to diagnose and treat (15) Abscess in the thoracic cavity Clairmont rejects primary cecostomy and reserves enterostomy for the complications He believes that hopelessly advanced cases of peritonitis are best treated conservatively

Appendicocecostomy—For the past 30 years the use of cecostomy or appendicocecostomy has been advised in the

treatment of peritonitis due to appendicitis Reeves²⁹ points out that marked distention of the cecum and colon is immediately relieved, bowel circulation is re-established, the mucous membrane approaches normal and that salme absorption is greatest, leading to dilution of toxins. In 52 cases where cecostomy or appendicocostomy was done there were 6 deaths or a mortality rate of 12 per cent. This compares tayorably with statistics of Finney, Jr. 240 cases of ruptured appendix, 50 deaths, 228 per cent Sworn and Fitzgibbon, 231 with 19 per cent mortality. He feels that this procedure has many advantages and no undesirable effects. It is to be recommended as a form of treatment

Silverberg³⁰ believes that decompression by means of eccostomy or appendicoeccostomy is of value and an aid to nature in treating these difficult cases of peritonitis.

Children — The treatment of peritonitis due to acute appendicitis by the

conservative method of Oschner is not advised by most men. The reason being that localization is not as effective due to the short omentum, that children do not tolerate tube drainage as well as adults, and that it is more difficult to obtain co-operation so far as complete rest is concerned.

Ladd³¹ reports a mortality of 3.5 per cent for 632 cases of acute appendicitis in children, and 7.3 per cent mortality for 204 cases of gross rupture of the appendix. The procedure followed has been immediate operation as soon as the child is properly prepared The profoundly toxic, dehydrated, distended patient with sunken eyes and a rapid feeble pulse is prepared for a day or 2 with parenteral fluids, transfusion, decompression and other measures before opera-The problem of immediate or tion delayed operative treatment is entirely a surgical problem to be decided in individual cases

A series of 181 cases in children with a final diagnosis of acute appendicitis which ruptured and resulted in a local or general peritonitis was reviewed by Elman 32 The mortality 15.5 per cent for the total cases, 6 per cent for the "nontoxic" group and 57 per cent for the 33 toxic cases. In arranging the cases according to the hour of operation, the mortality shows no consistent trend in the groups operated upon at various intervals following admission. However, there was a significant difference in mortality noted in the toxic cases where delayed operation was practiced. A mortality of 70 per cent in children operated upon at once, in contrast to 30 per cent in those operated upon from 9 to 24 hours later

It is pointed out that expectant or nonoperative therapy is reserved for a really small percentage of patients who should not have developed peritonitis. The necessity for immediate operation is clear whether the appendix is ruptured or not, and whether a peritonitis is present or not, provided the child is in a good condition to withstand the operation. Thus the question of immediate or delayed treatment in children is answered not so much by an estimate of the extent of the lesion, but upon the extent to which the lesion has affected the general condition of the child

Postoperative Complications—During 5 years, 36 patients complained to Pieri³³ of persistent pain in the right iliac fossa after an appendectomy for either chronic or acute appendicitis the majority of cases this pain began several hours after meals. The roentgen study of the cecal region failed to show any pathologic changes in the cecum Operation showed postoperative adhesions to be the case in 4 cases, recovery followed removal In 32 patients, one of various pathologic conditions (chronic colitis, simple, tuberculous or acute typhlitis or ilectyphlitis, mobile or atonic cecum and cecal neuralgia) ex-Resection of a segment of the ileocolic plexus between 2 ligatures induced recovery of the patients as determined by follow-up observation operation is known by his name in Italy and permanent satisfactory results have been reported from several hospitals

The importance of recognizing and properly treating hyperthyroidism as a pre- or postoperative complication of any surgical procedure is emphasized by the cases reported by Mora and Pearlman ³⁴. The patient, a female, 23 years, was known to have had hyperthyroid symptoms for 3 years when she was seized with acute appendicitis. After preparation with sodium iodide, dextrose, and saline intravenously and adequate sedation an acute suppurative appendix was removed. Adequate postoperative

treatment of the hyperthyroidism was followed by cure, and the gotter was removed 6 weeks after with success.

The possibility of appendiceal involvement in the typhoid group is mentioned by Hawkes.³⁵ It seems to be more frequent in the past few years with paratyphoid B, than with other organisms of the group. The involvement of the appendix may occur at any time during the disease, when it occurs early in the illness the picture is confusing. The treatment is the same as that of other types of appendicitis, vis., operation. He reports a case of perforation of the appendix for which appendectomy was done, that was followed by paratyphoid fever.

Gas gangrene of the abdominal wall is a rare and frequently fatal postoperative complication of acute appendicitis Smith and Zimring⁸⁶ report a case which was fatal in 5 days after appendectomy in spite of having received 71,100 units of gas serum and 5000 units of tetanus and gas bacillus antitoxin

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SPLEEN AND PERITONEUM

By Francis L. Zaborowski, M.D.

SPLEEN

Cystic Disease of the Spleen

B. Sherwin, et al., 1 report a case in a woman 46 years of age. There was no evidence of abdominal trauma. The spleen weighed 50 ounces (1500 Gm.); upon section, 4 cystic areas, varying in size and shape, and without a distinct lining membrane, were found There were irregular, friable, nodular masses which projected into the lumen of the cyst from all sides, which suggested that the cavities had been formed by disintegration of the previously solid parenchyma

Splenectomy in Blood Disorders

W. DeW. Andrus and C. W. Holman² report on 50 cases in which splenectomy was done By removing the spleen in hemolytic jaundice only a portion of the cells responsible, but a sufficient portion to restore a more nearly normal balance between blood formation and blood destruction in most cases, is removed Patients with definite thrombocytopenic purpura in the acute form are not good operative risks, and should be operated upon as a last resort Repeated blood transfusions may arrest the hemorrhage or even bring about an enduring remission of the disease injection of ascorbic acid is sometimes capable of producing remarkable improvement or remission Splenectomy was performed in 2 cases of atypical hemorrhagic purpura, atypical in that thrombopenia was absent. In one, a boy of 14, who had had symptoms of hemorrhage, purpura and the development of ecchymosis from slight trauma for 8 months, a good result was obtained. The other patient was a 39-year-old woman

who showed no improvement after splenectomy. The removal of the spleen in Banti's disease seems definitely warranted in the early stages and may alleviate some of the symptoms over a considerable period. The benefit which results would seem to be due to the reduction of the amount of blood coming to the liver through the portal vein which follows splenectomy. In many cases the platelets reach high levels after operation and thromboses are common. There were no operative deaths in 8 cases, but 1 patient died 2 years after operation of progressing cirrhosis with ascites. In 4 cases of erythroblastic (Cooley's) anemia there were no operative deaths but 2 of the children have since died, one 8 months and one 2 years after operation. of progressive anemia and pneumonia. The other 2 children are living 3½ and 4 years after operation, but both have erythrocyte counts of slightly over 3.-000,000 cells, and hemoglobin values around 50 per cent. In 3 cases of aplastic anemia, splenectomy did not alter the course of the disease. Splenectomy was also performed on a child with nonlipoid histiocytosis. The operation apparently discomfort somewhat the alleviated caused by the spleen and temporarily relieved the purpuric manifestations but did not arrest the progress of the disease Splenectomy in 1 case of leukemia did not improve the condition

Value of Splenectomy—D C Collins³ studied the outcome of 81 splenectomies. He finds it is the only proper treatment for traumatic rupture of the spleen, essential chronic thrombopenic purpura and congenital hemolytic icterus. Its value in early Banti's disease is less clearly defined. Elective splenectomy in

sickle cell anemia, Gaucher's disease, malaria and early portal cirrhosis with splenomegaly, is not usually advisable Splenectomy is usually contraindicated in polycythemia vera, syphilis, Hodgkin's disease, tuberculosis, the leukemias or radiosensitive splenomegalies.

MESENTERY

The Common Mesentery

By commen mesentery is meant a disturbance of the dynamic evolution of the median loop so that there is a failure of coalescence of the mesentery with the parietal peritoneum A Previtera4 divides the cases into 4 groups. In group I there may be failure of intestinal rotation where the small intestine remains in front of the colon, with the duodenojejunal flexure in the midline Here the splenic flexure is lacking and the small intestine, cecum, and ascendin colon are attached by a common mesentery to the posterior abdominal wall. In group II, with incomplete rotation, the small intestine is situated to the right and the colon to the left of the midline. In group III there is an inverted rotation of the umbilical loop Group IV includes cases in which there is a perverted rotation of the median loop of bowel. The author concludes that the common mesentery depends most often on disturbed rotation of the umbilical loop of bowel. The commonest symptoms are of a mechanical nature as characterized by volvulus, torsion, and invagination. Surgical treatment aims at restoration of normal conditions to the intestinal attachments, according to the findings in the individual case

Mesenteric Cysts

According to Babcock, these arise from. (1) Misplaced remnants of the

wolffian body or mullerian duct; (2) hemorrhage (serous cysts, serosangumous cysts), (3) obstructed and dilated lymph spaces (chylous cysts) They may be true cysts and pseudocysts. Pseudocysts arise from trauma, hemorrhage, degenerative changes, inflammation and from other cystic tumors. The pseudocyst walls are made up almost exclusively of connective tissue Cysts have been classified by E Fiorini as (1) Lymphatic cysts; (2) enteroid cysts, (3) wolffian cysts, (4) dermoid cysts, (5) teratoid cysts, (6) parasitic, as echinococcus and cysticercus cysts, and (7) gaseous cysts. These cysts are most commonly encountered in individuals from 5 to 25 and are found to involve the mesentery of the small intestine and especially the terminal portion of the ileum Females are more frequently affected than males. The cyst may have 1 or several cavities. These cavities communicate with one another and contain usually a clear vellowish or opalescent milkish-white fluid. The cyst wall is made up of 3 layers, an external one continuous with the peritoneal serosa and made up of adult connective tissue, a middle one made up of young connective tissue containing many blood vessels and lymphatic spaces and an internal one made up of endothelial cells arranged in a mosaiclike fashion The fluid in the cavity contains albuminoid and fatty substances, salts, and certain extractives whose proportions vary according to whether the liquid is lymph or chyle

Symptoms—\arious gastrointestinal disturbances such as nausea, abdominal distention and constipation are common. An abdominal tumor may be visible. The most important sign is intermittent abdominal pain due to torsion, pressure and to a reduction in the caliber of the intestinal lumen. One may be able to palpate a fluctuating mass. L

Costa⁶ reports a case in a 5-year-old boy, who presented the picture of an acute abdomen The signs were referable to the right lower quadrant of the abdomen The child suffered similar attacks previously, especially in winter. The prognosis is bad in untreated cases The condition should be differentiated from (1) Retroperatoneal tumors; (2) pedunculated ovarian cysts, (3) intestinal tumors, (4) hydropic degeneration of the gall-bladder, (5) cystic tumors of the pancreas, (6) pedunculated cysts of the liver and of the spleen, (7) neoplasms of the omentum and mesocolon and (8) pelvic neoplasms. The treatment is surgical removal.

Suppurative Adenitis of the Mesentery

Microorganisms reach the mesenteric lymphatic system by way of the blood stream, by way of the general lymphatic circulation, or by extension of regional lesions involving the intestine and its serosa F Larghero Ibarz⁷ distinguishes 5 principal types of lesions (1) Solitary, single, enlarged lymph glands, ranging from the size of a nut to that of a hen's egg. The mass is usually fluctuating and contains, as a rule, fluid pus (2) Multiple lymph glands which appear enlarged and edematous. Usually 1 of them is the seat of abscess formation (3) Multiple involvement of the lymph glands showing confluence. The suppuration of this mass usually gives rise to multiple abscess formation (4) Multiple involvement of solitary lymph glands which present merely a hypertrophy, but which on sectioning are found to contain multiple (5) Lesions bearing microabscesses grossly a striking resemblance to neoplastic formation

Suppuration of the mesenteric lymph glands may lead to the following processes and complications. (1) Cyst forma-

tion with subsequent absorption, which may be so complete as to leave little or no trace of the original lesion. (2) Formation of a tumorlike mass situated usually in the ileocolic recess or at the foot of the mesentery This lesion may be so small as to escape detection during clinical, surgical, or post-mortem examination (3) Purulent or fibrinopurulent peritonitis of various degrees of severity determined by the rupture of an intralymphatic abscess or by the propagation of an adjacent suppurative process (4) Intestinal occlusion determined either by pressure or by the formation of adhesions (5) Localized peritonitis. (6) Massive invasion of the entire mesenteric lymphatic gland system. (1) Extension into the liver with the formation of multiple hepatic abscesses (8) Suppurative periadenitis followed by an infiltration of the mesentery or mesoappendix. In these cases the mesentery becomes markedly thickened (9) Subphrenic abscess

The factors leading to this condition may be briefly subdivided into the following groups (1) Jejunoileal lesions; (2) lesions of the vermiform process; (3) lesions of the cecum; and (4) bloodstream infections. He stresses the fact that of all the intestinal lesions, acute appendicitis is most apt to produce suppurative changes in the mesenteric lymph gland system.

Treatment—This consists essentially in removal of the underlying cause and raising of the natural defense mechanism of the body

Mesenteric Lymphadenitis

This occurs in children and adolescents between the ages of 6 and 15. Occasionally it is seen in the adult. Males seem to be affected more frequently than females. Wise⁸ noticed a late summer incidence and uniform recovery after

appendectomy in his cases. Many writers have attempted to show association of the enlarged mesenteric nodes and upper The evidence respiratory infections. seems to point to a virus or a toxin but has not been definitely proven, and infection in some cases has been proven pres-White and Collins feel that the condition is a virus disease and offer the interesting suggestion that it may represent an abortive type or stage of infantile paralysis. They have noticed a similarity of lymphadenopathy found in cases of poliomyelitis, with some similarity of the abdominal symptoms. Gage has seen enlarged mesenteric lymph nodes in about 60 per cent of his cases of chronic appendicitis. The bacterial flora of these nodes was investigated and the enterococcus was obtained in 93 per cent of the nodes cultured Some authors still feel that the so-called adenopathy may be a phase of tuberculosis

Symptoms—The symptoms are acute and chronic In the acute form, pain is always present. It is in the right lower quadrant of the abdomen and radiates to the left of the abdomen along the root of the mesentery of the small bowel. The pain is usually cramplike or colicky and occasionally sharp. Nausea and vonuting are common Tenderness in the right lower quadrant of the abdomen is always present. In the chronic form, the symptoms are those of chronic appendicitis and in addition pain on pressure along the route of the mesentery of the small bowel

Diagnosis—It is difficult to differentiate the acute form from acute appendicuts. In addition to the signs and symptoms. Klein⁹ suggests that turning the patient from side to side causes a shift of the area of tenderness, differing in this from appendicitis as the cecum is more fixed than the mesentery. A. Ochsner and S. D. Murray¹⁰ stress the pres-

ence of tenderness along the root of the mesentery, *i. e.*, on a line extending from McBurney's point upward and to the left of the umbilicus.

Treatment—Evident foci of infection should be remedied, a proper dietary régime carried out, and all other appropriate hygienic and medical measures seen to Some calcified nodes may be removed *Appendectomy* is productive of good results.

OMENTUM

Internal Strangulation Through the Greater Omentum

F. Luccioni and N. Thomas¹¹ reviewed the literature and found only 35 cases of herniation of the bowel through an orifice in an otherwise normal, normally placed greater omentum. This rare anatomical defect is usually found singly; infrequently there are 2 or more rents in the membrane The opening may be from 1 to several centimeters in diameter and its edges may be thin, as is the case after a fresh mechanical rupture, or they may be thickened and adherent to parietes or intestines if the defect is the site of a chronic inflammatory process. If the latter is the case, the orifice presents a setting especially adapted to the strangulation of a loop of small bowel Because of its long mesentery, its peristaltic movement, its small size, and its freedom of movement in the abdominal cavity, the small bowel is almost invariably found to be strangulated in such an opening. Only 1 case of colonic strangulation has been reported Three types of "transepiploic" hernias may be distinguished: (1) The intestine passes through an orifice of the omentum already contained in the sac of an umbilical, inguinal, or femoral hernia; (2) the intestine gains access through an operative defect of the

omentum, as after an anterior gastroenterostomy; (3) the intestine passes through a thinned out area of a normal omentum. Such strangulations may be caused by the increase of intraabdominal pressure, as in defecation, micturition, and parturition. The symptoms are those of a subacute mechanical intestinal obstruction, with gradually increasing pain, vomiting becoming fecal, distention, fluid collection in the flanks, and other common signs of ileus, together with an increase in the fever and pulse rate, and, finally, oliguria Unless the diagnosis is made and surgical intervention is resorted to early, these patients usually die of generalized peritonitis following a gangrenous slough of the trapped coil of intestine. Unfortunately the diagnosis is frequently not made, and surgical relief arrives too late or not at all.

Cyst of Omentum, Mesentery and Retroperitoneum

L Berger and R E Rothenberg¹² believe that omental, mesenteric, and retroperitoneal cysts should be grouped as one, that is, retroperitoneal, since embryologically and pathologically they have a similar origin. Symptoms and signs are acute or chronic The acute symptoms are often occasioned by hemorrhage into the cyst or rupture of the cystic wall The chronic symptoms are usually mild, the main complaint being that of a progressively growing abdominal tumor Albummuria was observed in 9 cases The exclusion, by x-ray examination, of the gastrointestinal and urinary tracts as the seat of the pathologic changes is helpful in establishing the diagnosis of omental, mesenteric or retroperitoneal cyst Omental cysts are usually large, thin walled, multiloculated, and contain serosanguineous fluid They tend to rupture easily, thus causing acute symptoms

Mesenteric cysts are often the size of a grapefruit, are thick walled, do not rupture easily but tend to cause intestinal obstruction. If they arise from the mesentery of the small intestine, they usually contain chylous fluid. Cysts arising from behind the posterior peritoneum grow to huge dimensions, are thin walled, rupture occasionally and most often contain straw-colored or serosanguineous fluid. Microscopically, the commonest observations are either a cystic wall composed of loose fibrous tissue or a flat endothelial layer surrounded by a fibrous layer of tissue Whenever possible, complete resection should be performed but, if hazardous, then marsupialization or simple incision and drainage of the cyst is sufficient. These cysts show little tendency to recur or to become malignant. Extensive surgical intervention was not necessary, the authors state, since complications did not occur in their patients.

Primary Acute Epiploitis

The term epiploon is applied not only to the great omentum, but also to the gastrocolic omentum, the gastrohepatic omentum, and the numerous epiploic appendages found on the large intestines. Acute epiploitis is primary when there is no known etiology. If the epiploon is caught in a hernial sac, or involved in the adhesions of a previous operation or adjacent diseased organ, it is considered secondary. E. L. Eliason and J. Johnson¹³ reporting on 13 cases, found 8 of the patients to be males. The age varied from 20 to 62 years. There were no children in their series.

Etiology — Primary acute epiploitis could result from (a) strangulation by torsion of the epiploon, (b) interference with the blood supply by embolus or thrombosis, or (c) bacterial invasion of the epiploon through the circulation or

from the adjacent intestinal tract. The etiological possibilities of the torsion may be. (1) There is sudden rotation of the body on violent exertion; (2) there is often a congenital malformation of the omentum so that the part involved is long and narrow and therefore easily twisted on itself, (3) the anatomic arrangement of the vessels may be such that the long tortuous veins twist around the short arteries as the omentum swings from the transverse colon, (4) venous thrombosis may be the first lesion. The veins would then become distended and would easily rotate around the arteries Thrombosis of the vessels is always found at operation, but it cannot be demonstrated that it was present before the torsion, (5) an inflammatory process starts first and the torsion follows as the heavy inflamed omentum swings from the unaffected area, (6) the omentum, heavy with fat, is a good subject for torsion, as it swings from the transverse colon Farr and Bachman¹⁴ have suggested that torsion is more apt to occur in well-nourished individuals

Pathology—The torsion is the original incident and thrombosis and strangulation follow this. The torsion may be clockwise and counterclockwise. There is the usual picture of strangulation with damage to the blood vessel walls and extravasation of blood into the tissues. Fire, bloody fluid is found in the peritoneal cavity.

Symptoms—The symptoms were not diagnostic and resembled acute appendicitis. In 5 instances the pain was generalized and later localized from the start and remained so. The severity of the pain depends largely upon the size of the strangulating epiploon. Tenderness was present in all cases, rigidity in all but 3. Six had a palpable mass. The findings were on the right side of the abdomen in 10 of the 13 cases. The patients had very

little fever and all except one had a leukocytosis over 10,000.

Diagnosis—The diagnosis is usually made at operation.

Treatment—The treatment is resection of the involved epiploon.

Fibromyoma of the Omentum

Only 7 instances of this condition have been recorded in the literature. In most of the cases reported associated fibroinvoluta of the uterus were noted. Some believe that such tumors originate as subserous uterine fibroids which later became enveloped by the omentum, receive a collateral circulation from the omentum and ultimately are detached from the original host. In 2 of these cases the tumor was attached to the omentum by a cordlike structure which was highly vascularized In 1 case at operation, a torsion of the pedicle was found Under normal conditions, the tumors can be palpated. They are freely movable and situated in the region of the epigastrium W Jennings¹⁵ reports a case in a colored, married, 30-year-old woman, who complained of a sovere pain in the abdomen, which began 24 hours previously in the right lower quadrant of the abdomen She had several similar attacks during the past 2 years. The abdomen was rigid all over with tenderness most pronounced in the right side. Pelvic examination indicated a fibromyoma of the uterus Manipulation of the uterus and cervix caused pain At operation a structure like an umbilical cord was found extending from a short omentum to a semisolid tumor the size of a grapefruit

Treatment—Surgical removal.

PERITONEUM

Peritonitis

Circulatory Problems in Peritonitis—P. Windfeld¹⁶ studying circulatory

disturbances in peritonitis found the rhythmic movements of the intestine appear to influence the circulation in the portal system, but strong emphasis must be laid on the probability of separate movement of the intestinal mucous membrane. The rise of the blood pressure occurring in connection with peritonitis

pronounced in the musculature, and which denotes a general intoxication of the disordered organism.

Puerperal Peritonitis — Of the 28 cases of puerperal peritonitis reported by P. Balard, 17 16 occurred after abortion, the remaining 12 after delivery at term. At operation an incision was made in the

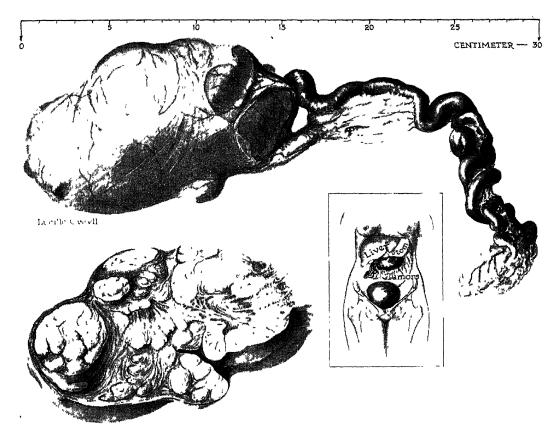


Fig. 1—Fibromyoma of omentum with cordlike pedicle. Insert shows relationship to other abdominal organs. (Jennings. Ann. Surg.)

is a consequence of the meteorism, and is accounted for by the compression of the intestinal capillaries, with the contingent reduced passage of blood through the portal system. The meteorism develops in the incipient stage of peritoritis at a time when we have no dependable evidence of a circulatory insufficiency with stasis in the portal system. The tardy fall in the blood pressure and the circulatory insufficiency are due to a universal capillary paresis which is particularly

lower portion of the abdomen and drainage was established, in most of the author's cases, a Mickulicz drain was used. While hysterectomy may appear to be a logical procedure in these cases, it involves too great a risk. Of the 16 patients in whom peritonitis developed following abortion, 12 died and 4 recovered. Of the 12 patients in whom peritonitis developed following delivery at term, 6 died and 6 recovered. After abortion the peritonitis was more frequently

secondary to a septicemia. The strepto-coccus was the organism most frequently found. F. Holtz¹⁸ collected a material of 176 cases, 100 of which had been treated by laparotomy and drainage. Only 20 of the patients survived.

Encapsulating Peritonitis — Etiology — Gastric hypoacidity, congenital malformation, a constitutional tendency toward fibrous tissue formation, previous operative trauma, accidental trauma, colitis, chronic appendicitis, adnexal disease, "internal hernia," acute peritonitis, and syphilis have all been proposed as the etiological basis for encapsulating peritonitis. The authors find peritoneal or pulmonary tuberculosis existing in almost every case of encapsulating peritonitis.

Diagnosis—In a patient who has had ascites or other tuberculous pleuroperitoneal antecedents, who has in the recent past shown signs of incomplete intestinal obstruction and who upon examination presents a soft or flabby mass, encapsulating peritonitis of tuberculous origin must be considered

Treatment—R Leibovici and B Y Yovanovitch¹⁹ report 6 cases and prefer not to remove the mass unless it is in a state of chronic quiescence. In such a case, if a bowel obstruction is present or threatening, they may attempt careful dissection followed by irradiation of the opened peritoneal cavity. In any other case, treatment is limited to irradiation. especially if there is any reason to believe that the mass is actively inflammatory. E Guipponi²⁰ reports 3 cases with partial involvement of the intestine and 1 with total encapsulation. He excised the membrane After excision, unlike ordinary adhesions, the membrane does not recur.

Experimental Background and the Clinical Application of the Escherichia Coli and Gum Tragacanth

Mixture (Coli-Bactragen) in Prevention of Peritonitis-B. Steinberg²¹ introduced Coli-Bactragen in 1 ounce (30 cc.) quantities intraperitoneally in the midline of the abdomen, a little below the umbilious, after the urinary bladder was evacuated. The material was injected from 12 to 96 hours prior to the operation in all but 16 instances in which it was poured into the peritoneal cavity at the completion of the operative procedure The peripheral leukocyte counts showed a continuous rise reaching the peak in from 24 to 36 hours. The average rise was a little over 10,000 leukocytes. The neutrophilic polymorphonuclears constituted from 90 to 98 per cent of the total number of cells and in the first 16 hours were of the mature In the following period, young forms appeared in the average proportion of 6 per cent. Smears and counts of the peritoneal exudate taken at operation, showed a variation in the number of cells from 73,000 to 210,000 per cubic millimeter. The neutrophilic polymorphoclears composed 98 per cent of the total number and at the end of 72 hours they still constituted 96 to 98 per cent. Young forms were found to vary from 6 to 11 per cent in 24 hours with a slight increase in their number in 48 and 72 hours. The appearance of the peritoneum varied from a moderate injection to an extensive fibrinopurulent exudate covering the peritoneal surfaces with a thick, gray fluid filling the pelvic cavity and The more pronounced the the flanks peritoneal reaction, the greater were the number of peritoneal cells and the higher the peripheral count. There was no apparent correlation between the intensity of the peritoneal picture and the age, sex. or character of disease. In the 391 patients whose records are analyzed here, the convalescence and recovery was uneventful. The possibility of formation of peritoneal adhesions due to the presence of the exudate in the peritoneal cavity is a pertinent question.

In 2 patients who were reoperated 6 weeks and 2 months respectively after the first operation at which they had Coli-Bactragen, no adhesions were found. Forty-six patients were followed up for a period of 3 years and no clinical manifestations of the presence of adhesions were observed Abdominal pain and distention followed by nausea and occasionally vomiting appeared approximately $2\frac{1}{2}$ hours after the peritoneal injection. The temperature usually rose 4° F. (2°C) with a corresponding increase in the pulse rate At the height of fever, the patient had a chill. These symptoms were occasionally entirely absent, or varied in degree and disappeared in 24 to 48 hours. When Coli-Bactragen was poured in during the operation, the reaction was completely masked by the anesthetic and the postoperative course did not appear to be adversely influenced. The cause of the reactions in people was determined accidentally. In an attempt to inject a very obese individual before operation, the material was introduced into the abdominal wall. No reaction followed When the error was realized. another injection, this time intraperitoneally, was made. The patient responded with the usual reactive symptoms is apparent that the mere irritating presence of a foreign substance in the peritoneum, and not some toxic action of the ingredients of Coli-Bactragen, is responsible for the reaction

Delayed Intervention in Appendiceal Abscess and Spreading Peritonitis Due to Appendicitis—H. K. Ransom²² classifies the following types of acute appendicitis with perforation for which delayed operation may be employed. (1) Cases with localized inflammatory infiltration A longer period of

time has elapsed following the perforation, the patient being seen on the third, fourth, or fifth day of the disease. The defensive mechanisms of the peritoneum have had a chance to begin their combat against the spread of the infection in the effort to wall off the process from the general peritoneal cavity. Drainage operations accomplish little, since there is little or nothing to drain. Appendectomy is hazardous, because protective barriers are broken down with consequent spread of the infection, producing a generalized peritonitis. (2) Cases of appendix abscess. In these cases the fact that the peritonitis is circumscribed and localized is indicative of a satisfactory resistance to the infection (3) Cases of general peritonitis. Here, because of low resistance on the part of the host, or a particularly virulent organism or combination of organisms, localization of the infection does not occur.

Babcock²³ believes operation that should be delayed in (1) Those with an initial or secondary chill, indicating that toxic infectious material is entering the blood stream or raising the question of the existence of a pylephlebitis; (2) those exhibiting the occurrence of diarrhea, which is often indicative of a very septic type of appendicitis, quite likely to be due to a virulent, streptococcal, or pneumococcal infection, (3) those showing mental excitation, delirium, or coma, (4) those with clammy skin, cold extremities, high rectal temperature, with black or yellow offensive vomitus, and (5) those with an abscess in the process However, when a sudof localization den lull in the symptoms occurs he advises prompt operation He remarks that in cases more than 48 hours old, and in which there is evidence of much free pus in the abdomen, much of this pus will be absorbed and an abscess will form about the appendix under a régime of

absolute rest. If, however, the patient is very toxic or there is a spreading peritonitis, and any operation is to be performed, simple drainage without search for the appendix is advised. He prefers for this a small muscle-splitting incision. In localized abscesses in the right lower quadrant he urges extraperitoneal drainage through a muscle-splitting incision, warning against drainage through the peritoneal cavity. For larger abscesses in the lower pelvis, drainage through the rectum is recommended.

Peritoneoscopy

A Critical Survey of Peritoneoscopy—E T Thieme²⁴ reports the result of observations carried out in 50 selected cases. It is so accurate that it has come to be considered a valuable final authority in diagnosis, which supplies much of the information usually gained by laparotomy with only a fraction of the expense and morbidity of a major opera-The technic employed was essentially that described by Ruddock tients were prepared as for laparotomy and all examinations were carried out aseptically. In order to allow more room for observation, an enema was given, which was followed by the administration of 1 cc of pitressin to reduce intestinal volume. Morphine sulfate was the only sedative used. One per cent of procame for local anesthesia was used, and only the site of puncture was anesthetized Local infiltration extended to all layers in an area of from 6 to 10 cm from the puncture site As a result, greater distention of the abdomen and painless manipulation of the instrument were possible. The incision was generally placed in the rectus muscle at the level of the umbilious. As a matter of routine. a nick in the fascia was made to facilitate the introduction of the large trocar. Room air of an unknown quantity and pressure were used for the pneumoperitoneum. In all instances the observations were successful, though occasionally limited by adhesions

Only cases that had been thoroughly

studied by other means were accepted

for peritoneoscopy, from which the proper diagnosis from an array of clinical possibilities presented by a large teaching staff was expected. The author divides the cases studied into the following general groups (1) Liver and spleen syndromes. (2) suspected abdominal malignancies. (3) unknown masses in the abdomen. (4) ascites of unknown origin, and (5) tuberculous peritonitis. With regard to the liver and spleen syndromes, the clinical diagnosis of jaundice or of hepatosplenomegaly can seldom be accurate. It must, however, be obtained to guide rational treatment. The problem is accurately answered by peritoneoscopy, and the therapeutic approach in jaundice and in hepatosplenomegalies is therefore indicated. With regard to abdominal malignancies, the author states that clinical findings alone cannot accurately disclose the moperable carcinoma of the stomach and peritoneoscopy should be used routinely to aveit operation in moperable As to the identification of unknown masses in the abdomen, peritoneoscopy must be recommended with reservations. The extent of pelvic and abdominal neoplasms can be accurately estimated for proper treatment, but peritoneoscopy cannot be expected to identify retroperitoneal masses unless they are far advanced Referring to ascites of unknown origin, the author states that with thorough clinical study before peritoneoscopy the group of ascites of unknown origin will continue to be small, but that peritoneoscopy may be expected

to give the correct diagnosis. Abdom-

inal tuberculosis can be readily diagnosed

and its course should be followed by repeated peritoneoscopic examinations

Spontaneous Hemoperitoneum in Men

H. Mondor and C. Olivier²⁵ reviewed 400 cases of hemoperatoneum in men and The most frequent site of the bleeding is in the spleen or one of its large vessels, but spontaneous rupture of any mesenteric, hepatic, or gastric artery, or even of the abdominal aorta itself, is also a possibility The clinical picture must be thought of in terms of chronology, as the symptoms change with time. First there is usually upper abdominal pain, but as a rule there is not much change in the pulse or temperature With the passing of time there may be some increase in the temperature, variable pulse changes, increasing pain, the appearance of abdominal rigidity or distention, and, occasionally, vomiting The temptation is to diagnose the condition as a ruptured peptic ulcer, or, less likely. intraabdominal mesenteric herma or volvulus, or bowel obstruction of undetermined origin. Almost invariably the incision should be made "above the level of the umbilious," and the surgical procedure should be one directed to the discovery of the site of the bleeding This task is always more difficult in the upper abdomen than it is in the pelvis

Primary Retroperitoneal Tumors

R T Frank²⁶ found reported in the literature 107 primary retroperitoneal tumors. The majority of the growths were mesodermal in origin (72 per cent), while 18.7 per cent were ectodermal (neurogenic), and 9.3 per cent were teratomas. The retroperitoneal tumor may vary greatly in size, 1 tumor, as noted in the literature, weighed 69 pounds (31.3 kg.). Such tumors may be solid or cystic and, with exception of the

round-cell sarcomas, are well encapsulated. Multiple masses, often unconnected, may be present, and the failure to remove all such masses is believed by the author to be responsible for the recurrence of the benign tumors. Histologically, these tumors fall into the following groups Lipomas; fibromas, cysts, myxomas, sarcomas, neuromas, and tera-In the author's series of 107 cases, recurrence was noted in 13 per cent, with metastases in 3.7 per cent, while in an older series metastases occurred in 33 per cent of the cases While the clinical symptoms are not characteristic, vague digestive disturbances, an abdominal mass, and loss of weight and strength are the rule. Most often the preoperative diagnosis is that of fibroids, ovarian cysts, hypernephroma, and tuberculous peritonitis Gastrointestinal and renal x-ray studies are of great value, both for exclusion and as a means of locating the tumor.

Treatment—Operation is the treatment of choice, and it is important that even benign growths be prevented from increasing to great size, or death will be the probable outcome. Only 101 per cent of the patients seen clinically were moperable Radiotherapy combined with surgery or used alone is valuable except in the lipomas and fibromas. The method of approach has been both retroperitoneal and transperitoneal. The operative risk is more closely allied to the histology of the tumor than its size mortality rate was 0 for benign tumors. 18.2 per cent for myxomas, 22 per cent for neuromas, 28 1 per cent for sarcomas, and 367 per cent for teratomas author adds 3 new cases, the first an embryonic tumor of mesodermal origin, the second a myxoliposarcoma, and the third a retroperationeal cyst that the author does not consider mesenteric in origin.

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HERNIA

By Frederick A. Fiske, M D.

INGUINAL HERNIA

Anatomy — An anatomical study of the lower anterior abdominal wall was made by M. Cherner ¹ The investigation had to do with the divisions of the abdominal wall; the average pattern, the variations from the average pattern, and the effect of the variations on the potentiality for herma. He concludes that: (1) Complete failure of the abdominal wall in its resistance to intraabdominal pressure and herma formation is improbable, if not impossible, when an average pattern is present (2) Herma formation may occur as a structural and functional failure of the entire abdominal wall or of any part or division due to: (a) Deficiency in the musculature of the component parts of the abdominal wall, the result of extreme degeneration or transformation into fasciae or aponeurosis, which have little ability to resist pressure. (b) Variations in the component parts of the abdominal

wall of such degree that complete valvular closure even with maximum contraction is impossible (c) The occurrence of simultaneous variations in 2 or more components of the wall (d) Delayed or non-co-ordinated action of the components of the abdominal wall, resulting in a failure of compensation and a deficient valvular mechanism

After studying the length of the ingumal ligaments, the depth and width of the pelvis in 87 men suffering with inguinal herma of various types, E Rebustello² concluded that malformation of the pelvis predisposes to the development of herma. He found that the mguinal ligaments of those with herma were longer than the control group of normal individuals the same age (14 cm or more and 10.5 cm, respectively). Harris and White found that a herma occurring in a person whose inguinal ligament was 15 cm. or less was always the indirect type, while an inguinal ligaHERNIA 825

ment over 15 cm. is always associated with a direct type of inguinal hernia.

Etiology — The etiologic factors as classified by H. E. Stein³ are

- 1. Anatomic:
- A Patent processus vaginalis.
- B General or local tissue weaknesses, $e\ g$, chronic disease, split aponeurosis, weak transversalis fascia
- C Disproportion between the abdominal capacity and contents; $c\ g$, large tumors or ascites
 - D Long or low attached mesentery.
 - E. Large internal ring.
 - 2 Mechanical:

Increased intra-abdominal pressure from within or without.

3 Physiologic:

Inadequate trapdoor action of the internal oblique muscle.

Types—Interstitial—An interstitial hernia is one in which the sac lies between the transversalis fascia and transversalis muscle and the aponeurosis of the external oblique It is frequently, but not always, associated with a bilocular sac. A. O Wilensky and J D. Gordon⁴ report the case of a woman, 62, who at operation was found to have a single sac 3 inches long lying between the external oblique aponeurosis. It was resected Cure followed repair The importance of this type herma lies in the possibility of overlooking this portion of the sac when operating to cure an inguinal hernia, thus predisposing to immediate recurrence by failure to remove a preformed sac. This type hernia frequently becomes incarcerated or strangulated.

Congenital—The anatomy and various methods of handling the lower portion of the sac of a congenital inguinal herma is discussed by Stanley J Seeger. He directs attention to the possibility of replacing the testicle within the scrotum but outside of the cremaster muscle and fascia—a condition which leads to discomfort and malposition of the testicle

Inversion of the scrotum on the index finger will serve as a guide to the proper channel, thus insuring proper replacement of the testicle.

Direct — Attention is directed to a type of direct hernia which occurs through a small circular tendinous opening in the posterior wall of the inguinal canal, and has a distinct sac.⁶ This differs from the usual direct hernia, which has a diffuse bulge with a large opening in the transversalis fascia and is not hable to strangulation. He reports 3 cases of this type, 1 found at primary operation for a supposed indirect inguinal hernia, 1 in which strangulation of the Richter's type had occurred, and 1 in a recurrent right inguinal hernia In 2 of the cases the bladder wall formed a part of the sac. These cases were found in a group of 80 hernias The important factors brought out by these cases are That strangulation is more likely in this type hernia, that recurrences may result from overlooking a hernia of this type, and that care should be exercised in liberation of the medial aspect of these sacs.

Traumatic Hernia—An inguinal herma due to direct trauma is rare, and usually due to laceration of the protecting tissues Hernia from indirect trauma resulting in increased intra-abdominal pressure and protrusion into a preformed but closed sac is relatively common. The case reported by G. L. McWhorter⁷ illustrates an inguinal hernia resulting from direct trauma A male, 22, developed a left inguinal mass immediately after being struck by the handlebar of his motorcycle At examination induration and subcutaneous ecchymosis were present over an inguinal swelling which transmitted an impulse on coughing. Operation revealed a complete tear of the external oblique, internal oblique,

transversalis and deep fascia Induration of muscle fibers was noted Repair was made by the Bassini Method.

Treatment—Operative — According to R L. Ramos and C. C Burton,⁸ unilocular indirect hermas are common in children and very young adults, but rare in males above 30 years of age. The majority of their cases had a definite direct sac or locule, making it the bilocular combined direct and indirect

a domelike relaxation of the transversalis fascia which is closed by a purse-string suture as suggested by Andrews and Bissell; uniting the transversalis fascia to the inguinal ligament, suturing the lower or outer leaf of the external oblique aponeurosis to the transversalis fascia, and finally suturing the medial leaf of the external oblique aponeurosis to the lower or outer leaf. The cord is transplanted. Fine black silk is the su-

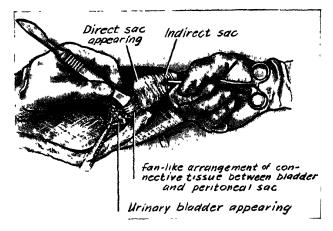


Fig. 1—Dissection has progressed. All direct sacs or locules have been dissected free. Notice the fan-like arrangement of peritoneum and bladder wall at this stage. (Ramos and Burton. Surg., Gynec. & Obst.)

They stress the importance of bidigital examination of the anterior and posterior surfaces of the inguinal canal in recognizing this anomaly. It is felt that many recurrences are due to overlooking these accessory locules at the time of operation. The importance of suturing like structures in contact without tension is emphasized. The unsound physiology of approximating unlike histological structures is criticized. In the technic which they describe emphasis must be placed upon complete dissection of the direct element by following down the indirect sac, then closure of the sac without transfixion, rebuilding the internal ring by uniting the muscle fibers of the transversalis and oblique muscles to each other under the cord, this forms

ture material used. This procedure is possible in all types of inguinal herma, including recurrent types.

R Pilcher⁹ advises the use of the plantaris tendon for repair of inguinal herma. The advantages claimed for this method are. The structure used as a graft is removed with very little trauma, and its removal causes no disability Being tendinous, the graft is probably less easily absorbed than fascia graft is inserted with minimal trauma to the structures between which it acts as a bridge. It is fixed without tension with unabsorbable sutures, this excites fibrosis which persists even if the graft is absorbed. Lateral stretching of the graft makes approximation of adjacent strands possible without tension

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The plantaris tendon is removed through a 1-inch incision over the medial aspect of the Achilles tendon a little above its lower end, then with a modified Mayo vein enucleator it is liberated to the upper end. A second incision is then made over the medial edge of the tibia, through which the upper end is divided.

After the usual exposure, treatment of the sac, and reinforcement of the

rowing the internal ring with mattress sutures placed above the cord, exposure and incision of the internal oblique aponeurosis at and parallel to its line of fusion with the external oblique to a point well above the internal ring, suturing the reflected internal oblique to Poupart's ligament with 3 chromic catgut sutures and a fascial strip taken from the medial leaflet of the external oblique aponeurosis, and union of the

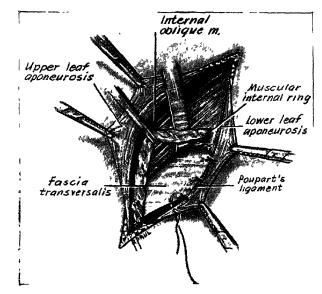


Fig 2—First stage of repair Fascia transversalis has been attached to Poupait's ligament Notice the first suture next to the cord which is muscular. This is the first fascial floor mentioned in operation. Internal oblique muscle is retracted. (Ramos and Burton. Surg., Gynec & Obst.)

transversalis fascia in the direct herma, the graft is sutured alternately to the inguinal ligament, and the conjoined tendon or one of its components with silk sutures. There is no tension on the graft. No attempt is made to join the conjoined tendon and the inguinal ligament. After the graft has thus been placed in a zigzag fashion the adjacent strands are sutured to each other, the lateral stretch allows this. In this manner a grid of strips is converted into the equivalent of a continuous fascial sheath.

The essential features in an operation which H E Stein³ describes are Nar-

edges of the external oblique usually under the cord. In the direct type of inguinal herma, he makes a longitudinal incision through the transversalis fascia, and sutures its free edge with the edge of the internal oblique to Poupart's ligament. The same procedure is used for recurrent hermas. Of 107 cases followed there were no recurrences in 62 indirect and 6 indirect-direct hermas, 3 recurrences in 26 direct hermas, and 1 recurrence in 13 secondary repairs. There was 1 death due to gangrene of the urinary bladder.

E H Carnes¹⁰ describes the technic of an operation for repair of direct in-

guinal hernia. The essential elements are closure of the transversalis fascia, transplantation of a fascial flap from the anterior rectus sheath, under the external oblique aponeurosis to the inguinal ligament by sutures of fascia lata, closure of the leaflets of external oblique aponeurosis over this with 2 layers of sutures by means of fascial sutures. In 100 cases the author had no infections

of woven fascia lata are used to bridge the defect

A method of repair of inguinal hernia which employs the fascial strips of external oblique aponeurosis as described by McArthur and the Halsted type of repair was described by L. Sacks. Stress is placed upon crossing the transplants over the cord and mutually transfixing them, then these are continued upward

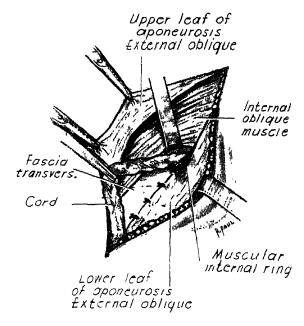


Fig 3—Second stage of the repair. The lower aponeurotic flap has been tacked on the fascia transversalis. This is the second fascial floor. The muscle is still retracted. (Ramos and Burton Surg., Gynee & Obst.)

of the wound, and while no recurrence has occurred he felt it was too early to draw conclusions

An operation for repair of direct herma, described by J. D. Bisgard, 11 transplants a flap of pectineus muscle and fascia upward over the transversalis fascia to the aponeurosis of the internal oblique and conjoined tendon. A second line of defense is made by suturing the internal oblique aponeurosis and conjoined tendon behind the cord to Poupart's ligament, with a pedicle strip of external aponeurosis. If undue tension has been caused by this union, strips

approximating the inguinal ligament to the conjoined tendon and internal oblique. The lateral leaflet of the external oblique is sutured to the internal oblique, and the medial leaflet to the lateral leaflet of the external oblique aponeurosis.

Studying the use of alloy steel wire sutures, which have been popularized by Babcock, L. R. Kaufman, W. W. Johnson, and A. Lesser¹² report the findings in a series of 56 consecutive herma operations. In Group I, 25 cases, catgut, chromicized and plain was used throughout for buried sutures; in Group II, 18 cases, alloy steel wire sutures were used

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for repair of anatomical defects but catgut was used for closure of the peritoneum; in Group III, 10 cases, alloy steel wire sutures were used for all sutures and ligatures, and in Group IV, 3 cases, black silk was used throughout. Analysis of these cases showed an incidence of infection of the wound in Group I of 24 per cent, Group II of 11 per cent, Group III none, Group IV 66%

necessary to consider the report of Burdick and Coley, who had 47 failures (81.03 per cent), 11 possible cures (18.96 per cent) and 2 probable cures (3.44 per cent) in 56 cases followed from a group of 66 cases, and the fatal cases due to perforation of the bowel reported by Berne.

Certain essentials in the technic of injection therapy are emphasized by

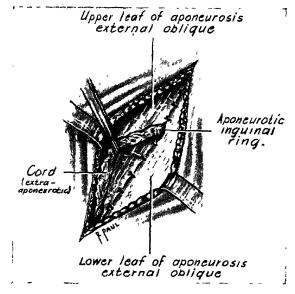


Fig 4—Last stage of the operation. The oblique muscle has been allowed to fall in normal place. The upper aponeurotic leaf has been attached to the lower aponeurotic leaf, creating a third tascial layer of the newly reconstructed floor. The cord finally is placed extra-aponeurotically (Ramos and Burton. Surg., Gynec. & Obst.)

per cent Seroma was noted as follows: Group I, 0, Group II, 5 (27 per cent); Group III, 0; Group IV, 1 (33 per cent). The degree of wound induration at the time of discharge from the hospital was less in both groups where wire had been used; however at follow-up (2 to 10 months) later no difference was noted. There were not enough cases to draw any conclusions as to recurrence rate

Injection—As a review of this method of treatment Table 1, compiled by H I. Biegeleisen and I. J Tartakow, ¹³ gives a good outlook on the status of the subject. To complete the picture it is

Biegeleisen and Tartakow. Careful study and visualization of the inguinal anatomy and type of hernia are important They consider the variation in location of the injection in the direct and indirect type of herma. The importance of keeping the needle pointed toward the pubic spine is re-emphasized and the site of deposit at each injection illustrated according to a definite routine As most others they advise primary obliteration around the internal ring and reinforcement of Hesselboch's triangle in both types of hernia. The importance of proper truss pressure continuously and the various types of truss are considered

TABLE 1

Date	Author	No ot Cases	Solutions Used	Method and Results	
18.5	Velpeau	3	Iodine	Flushed hernial sac through incision in scrotum, all 3 cases cured	
1836	Pancoast	13 in 8 yrs	Lugol's sclution Tr cantharides	Used syringe and cannula, all cured	
810	Jaynne		Essential oils Tr	Special patented instrument, claimed 75 per cent cures	
1811	H aton		Secret at first Sclution quercus all us	Special syringe and needle, distavor of American colleges due to secrecy of method, claimed too much (100 per cent cures (?)), only 1 injection given, patient put to bed and bandage applied	
1877	Schwalbe		70 per cent alcohol	Da ly injections for about 2 weeks, patient kept in bed	
88	W'arren		Quercus al ¹ us	Disciple of Heaton, only 1 massive dose given and patient confined to bed, first to describe rationale of seroglastic tissue repair, recommended painting inguinal rings and canal with solution during surgical operation (80 to 85 per cent cures)	
1892	Narv			Discussed injection treatment in monograph on herma	
189,	N anl v			Emphas zed proper selection of cases	
9,0	Pira Mestre	15,000 (20 yrs)	P na Mestre	(lans inguinal close lin 10 to 15 days (98 per cent cures)	
1900 to 1922	Ma er	2',000 (30 yrs.)	Zr sult then land alc bol	First o make treatment ambulant, 98 per cent cures, 2 per cent cured subsequency, small closes, patient work truss during treatment	
1004	W ll iman	224	Alcohol (2)	92 per cent cure	
1907	Lannelorgue		10 ret c nt zmc chlo- tide	Very enthusiastic about its use in hernia injec- tion after noting its effect on stimulating growth of fibrous tissue in tuberculous de- posits	
1928	Steffen	2775 (30 vrs.)	Meohel	One injection weekly for 1 year, no deaths in 30 years of treatment (91.2 per cent cures)	
92)	Win	Revi w of 4632	Medual	3084 follow-ups, 91 per cent cures, no vital damage, 4 per cent complications (abscess, orchitis, hydrocele, atrophy of testis)	
1929	Hall	33	Pipa Mestre	Histologic work on animals (peritoneal injections), formation of adhesions and a connective tissue barrier, thus effectively blocking and obliterating the canal, 1 failure	
1930	Goldbahn	-	Meohol	Reported results of unskilled injections in cas s of strangulated irreducible hermas, resulting in sepsis, fecal fistulas, and deaths	
1930	Jameson and Cantala	64	Pina Mestre	12 to 15 daily injections, claim it is the method of choice in cases of recurrent hernia	
1931	Wolte	22	Pina Mestre	Described scroplastic exudation and formation of adhesions in inguinal canal, injected into peritoneum of animals and produced plastic peritonitis, claimed vas not injured if cord injected	
1932	La Rochelle		Pina Mestre	Injections should supplement operative treat- ment, help produce internal tissue pad or truss	

TABLE 1—Continued

\(\Gate\)	Author	No ot Cases	Solutions Used	Method and Results	
,933	A cK nrey		Phenol, alcohol, oil of thuja	Production of fibroblasts (without necrosis) in adjoining muscle tissue	
1)34	l ars m	137	Phenol, alcohol, and thuja solution	8 injections, injection treatment suitable in 90 per cent of cases seen (93.5 per cent cures); no serious complication	
1 34	Grav	20	Mayer's solution	75 per cent cure	
1934	Branud	406	Tannic selution	4 per cent recurrences with 3 final failures, animal injections, marked fibroblast proliferation, no polymorphonuclears, giant cells, or necrosis	
1934	Rice	600	I henol, alcch(l, ard oil of thuja, sodium rsylliate	2 failures, no severe complications, histologic work on biopsy specimens from injected cases at operation shows dense adult fibrous tissue present by the forty-second day after injection	
1935	Cwl r	700 (5 yrs)	Tannic and gallic acids	98 per cent cure, no serious complications, advised initial overbuilding of tissue to allow for absorption	
1935	Fancus			Believes certain percentage of reducible herniz curable by injection	
1 35	Cuillin	242		210 indirect, 4 direct, 23 recurrent, 5 umbilical, work and investigation on cadaver	
1 735	Br tzsch nar	140		Points out injections close hernial sac same as nature closes processus vaginalis	
03)	McM llan	400	huja s lution, tan-	8 per cent recurrences, no serious complication	
1936	Z nan and Larkows'i	1	Tr of thuja	Report necrosis of cord structures with swelling of vas after 1 injection	
1936	Girard	174	Tan uc acid, phenol, ard alcohol thuja s lution sylnasol, Pina Mestre	Series included 19 postoperative recurrences also injected postoperative repairs with threatened weakening, claims recurrences in injected cases due to undertreatment	
1936	Gordon and Gordon	5		Contraindication of injection treatment in slid ing hernia, present in 1 2-1 5 per cent of case seen, injections, however, do not interfer with operative procedure or result	
1937	Crohn		Phon I, alcohol, and oil of thura	Confirmed Rice's histologic work, no serou complications	
1937	Rea			Reviewed 75 cases injected for unilateral in guinal hernia and found only 1 case of delain libido, followed 26 cases injected for it lateral inguinal hernia for 3 years and found normal spermatic count, no sterility	

(Biegeleisen and Tartakow Suigery)

Resilient, oval pads thickened at the upper end for indirect herma and at the lower end for direct herma are advised. They have used the method in 200 cases but do not give figures as to permanency of cure. The complications have been of a minor character, consisting of intraperitoneal injection, hydrocele of the tes-

ticle (5 cases), slight swelling of lymph nodes and cord

W. M. McMillan divided his cases into those 50 years or over, of these 133 hermas in 108 patients were treated, 76 indirect inguinal with 13 recurrences, 40 direct inguinal with 8 recurrences, 11 recurrent inguinal after surgical repair

with 2 recurrences, 2 incisional with 1 recurrence, 4 umbilical with 2 recurrences, giving a combined recurrence rate of 20 per cent in all cases over 50 years of age. Of 124 hernias treated in 94 patients under 50 years of age, 71 were indirect inguinal with 9 recurrences, 33 direct inguinal with 8 recurrences, 12 recurrent inguinal after surgical repair with 2 recurrences, 2 femoral with 1 recurrence, giving a combined recurrence rate of 16 per cent in all cases under 50 years of age. The average length of time since the last treatment was 2 years. There was no mortality. The complications were not serious: Swelling and pain of the cord not more than 1 day's duration, 5 cases were incapacitated from 1 to 12 hours, 3 had symptoms of peritoneal shock. This recurrence rate indicated that cases should be more carefully selected. He is advising surgery in all cases of large herma and cases with thin muscle and fascia

Postoperative Complications -2000 cases of simple indirect or direct mguinal herma studied by F. Beekman and J. E. Sullivan, 14 there were 1508 operations for single and 492 for bilateral hermas (2492 actual operations) In 321 cases (16 per cent) postoperative complications were noted (Table 2), with 5 deaths (025 per cent). All the deaths were in cases of single herma in men, 2 were due to pneumonia, and 3 to pulmonary emboli. Almost twice as many complications occurred in patients operated upon for bilateral hernia (231 per cent) as for single (137 per cent) There was a well marked increase in the complications from the third decade of life onward, which was also greater in the bilateral cases. Analysis of the wound infections was lowest where silk was used (27 per cent by cases, 23 per cent by wounds); catgut (49 per cent by

TABLE 2
Complications

	Cases	Per cent
Wound hematomas	17	0.8
Wound infection	99	4.9
Respiratory lesions .	171	8.5
Thrombophlebitis	6	0.3
Marked postoperative disten-		0.5
tion	6	0.3
Persistent headache (follow-		0.5
ing spinal anesthesia)	4	0.2
Iodine dermatitis	2 2	0.1
Cystitis	$\overline{2}$	0.1
Severe hiccoughing (local anes-		0.1
thesia)	1 1	0.05
Gastric dilatation (Spinal		0.00
anesthesia)	1 1	0.05
Postoperative psychosis (gen-		0.00
eral anesthesia)	1 1	0 05
Jaundice (spinal anesthesia)	1	0 05
Bacıllary dysentery	4	0.2
Measles	4 1 1	0.05
Scarlet fever		0 05
Mumps	1	0 05
Otitis media	1	0 05
Unexplained diairhea	1	0.05
Toxic erythema	1	0 05
	321	16 00
-		

(Beekman and Sullivan Surg, Gynec & Obst)

cases, 39 per cent by wounds); kanga-100 tendon or ox fascia (68 per cent by cases, 56 per cent by wounds), and highest with autogenous fascia (13.8 per cent by cases, 98 per cent by wounds). Of 171 (86 per cent) cases of respiratory complications, 71 (35 per cent) were serious, 46 cases of atelectasis (23 per cent), 13 cases of pneumonia (07 per cent), and 12 cases of pulmonary embolus (06 per cent). The respiratory complications were higher in the bilateral cases (126 per cent) than in the single cases (67 per cent) The cases of atelectasis appeared in all decades of life, the rate was lowest during the first 2 (04 and 12 per cent respectively) and remained the same (2.7 per cent) in the succeeding ones. Pneumonia was more common in the aged. There was not a single case of pulmonary embolus in 394 patients under 20 years of age, an incidence of 0.3 per cent occurred between

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the third and fourth decades, which increased to 13 per cent during the fifth, then fell to 0.8 per cent in the sixth, and finally reached a high of 34 per cent in persons over 59 years of age. There were 3 deaths in this group and 1 of these was in his fifth decade, and the other 2 were over 60 years of age. The length of time used in performing the operation played an important part in The wound infections complications. rose rapidly from 0.5 per cent for a 30-minute period to 25 per cent when the operation took longer than $1\frac{1}{2}$ hours. It was evident that the mild and serious respiratory complications were more frequent in longer operations. The incidence of wound complications was lowest with local anesthesia, next with general anesthesia, and highest with spinal. The type of anesthesia did not seem to affect the less serious respiratory infections, but it did affect the morbidity of the serious pulmonary complications: Atelectasis was twice as common when local and spinal were used, pneumonia was more than twice as common following the use of general anesthesia; embolus appeared as a complication onethird as often after spinal as it did after either general or local Thrombophlebitis was a complication in 6 cases and its frequency did not seem to be affected by the type of anesthesia or the suture material.

Recurring peritonitis following operative reduction of a strangulated inguinal herma is a complication which has been well emphasized by the case reported by R H Meade ¹⁵ The patient was first operated upon for a strangulated herma which was reduced and returned to the abdomen; during the next 15 months he had recurrent attacks of peritonitis for which 3 operations were done, finally a segment of ileum was resected at the fifth operation with apparent re-

hef of symptoms. The original hernia recurred and was repaired at a sixth operation. This case shows that primary resection may be the wisest procedure if there is doubt as to the viability of the bowel. It was thought that organisms spread through the distended walls of the diseased loop when tension became great enough.

FEMORAL HERNIA

During a 20-year period, 16 4530 operations for inguinal hernia and 90 operations for femoral hernia, or a ratio of 50 to 1, were reported. In the 90 cases, 54, or 60 per cent, were males, and 36, or 40 per cent, were females. This discrepancy is probably due to the industrial type of patients treated by them. The greatest number of patients, 76.7 per cent were between the ages of 30 and 60. Only 9 had worn a truss. A history of trauma in connection with the appearance of the hernia was obtained in 22 cases, 24.4 per cent Obesity did not appear to be a factor in the production Due to the small of femoral hernia number of cases, 36, of whom 14 had no pregnancies, the relationship of childbearing to the incidence of femoral her-In 21 cases, an ma was inconclusive operation for inguinal hernia had been performed This observation directs attention to the advisability of careful examination of the femoral region during inguinal hernia operations Operation was done within 1 year of the appearance of the herma in 578 per cent, only 11.1 per cent had the herma 5 years or longer The right side was involved more commonly than the left side, in a ratio of 70 to 30

Incarceration occurred in 21 cases, and 8 (36.4 per cent) of these showed interference with the blood supply of

the intestine. Resection of the bowel was necessary in 3 patients with 2 deaths. One other death due to shock occurred, giving mortality of 15.2 per cent for incarcerated and strangulated femoral hernias.

The femoral approach was used to repair 54 cases with 9.7 per cent recur-

peritoneal wall, and closure with a pursestring suture of black silk. In cases where adhesions or edema prevent liberation of the sac from above, it is suggested that the skin flap be retracted below Poupart's ligament, and the sac liberated below before inverting it above. The transversalis fascia is then divided

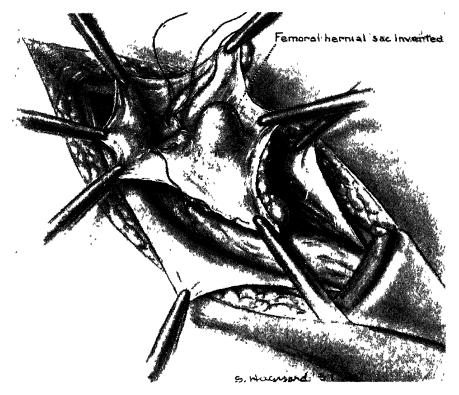


Fig. 5—A purse-string suture of silk is closing the peritoneum proximal to the neck of the temoral hermal sac. The latter will be cut away with the remaining redundant peritoneum. (McClure and Fallis. Ann. Surg.)

rence, 27 cases were repaired via the inguinal route with 74 per cent recurrence, and 9 cases were repaired by combining the femoral and inguinal approach with no recurrence. Although the inguinal approach is a more difficult procedure, the authors feel that it is preferable in all except the small femoral hermas. They suggest opening the inguinal canal in the usual method, isolation and opening the peritoneum at the region of the internal ring, inversion of the femoral sac by tractions on the medial

in Hesselboch's triangle, exposing the superior opening of the femoral canal which is closed. It is necessary to carefully repair the opening in the transversalis fascia.

An unusual case of gangrenous appendicitis occurring in a male with a right femoral hernia was reported Watson up to 1923 collected from the literature 181 cases of an appendix in a femoral hernial sac. McClure and Fallis were able to find 11 additional cases in American and British literature, bringing

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the total, including their case, to 193 cases; of these, only 6 were in males.

In this series, the complications were phlebitis, 2; pulmonary, 1; and wound infection, 1. An operative mortality was recorded in 4 cases, 4.4 per cent.

Perforation or rupture of normal intestine, transiently incarcerated, may result from force applied directly to the hernia and from contusion of vigorous attempts at reduction. The case reported by S. Mufson¹⁷ illustrated this point. A male, 57 years of age, who had a right femoral hernia 15 years, had sudden pain at the hernial site after it came out while lifting. He had considerable difficulty reducing it, and when it was reduced he felt something tear inside. This was followed by severe pain in lower left abdomen with nausea. At laparotomy 7 hours later, gangrene of the mesentery and ileum and a perforation of the ileum were found. Bowel resection with side-to-side anastomosis was done. No attempt to repair the femoral hernia was made. Recovery followed.

VENTRAL HERNIA

In 1934 Wangensteen described the use of pedicle flaps of iliotibial fascia for the repair of difficult ventral hernias. P Manjos and B L. Coley¹⁸ report a case of acquired interfascial bursa as a complication of this type repair. The patient, age 43 years, had a lower midline ventral hernia 3 years after a laparotomy, which recurred 3 months after an operation to repair it 7 years after the onset At operation in 1937, 1 year after the recurrence, the defect was closed, and a flap of iliotibial fascia attached at the proximal end was passed, subcutaneously upward, covering the closed Interrupted silk sutures were used Due to increasing pain, tenderness and swelling over the incision she was reoperated on 5 months later. An intact, tense, bulging fascial transplant was incised, liberating 25 cc. of straw-colored, clear, viscid fluid. The underlying rectus sheath was intact. In order to prevent the occurrence of this condition particular care should be taken to obliterate the dead space between the fascial transplant and the rectus sheaths.

Traumatic—According to W. Ehalt. 19 pure traumatic ruptures are extremely rare and always occur by direct trauma with all the symptoms, as swelling, hematoma, tenderness, and sometimes skin abrasions. Finding torn muscle at operation is also important. He reports the case of a man who was struck by a wagon tongue. A tumor the size of 2 men's fists at the level of the umbilicus at the outer border of the rectus immediately appeared. There were associated skin excornations and ecchymosis. After allowing the acute tissue damage to subside, a successful repair of the hernia was made

VAGINAL HERNIA

Vaginal hermia is a hermiation of the peritoneum pushing downward through the pelvic floor into the vaginal vault, or along the wall between the vagina and rectum or bladder, sometimes extending all the way to the permeum. It is a subvariety of pelvic hernia, which includes all hernias through the pelvic floor Hall reports a case in which microscopic examination of the involved tissues was made. It was indicated that aneurismal relaxation of degenerated tear tissue occurred as a result of obliterative endarteritis. The posterior types which occur in the bottom of the cul-de-sac, the internal ring being formed by the uterosacral ligaments and anterior rectal wall, or by separated fibers of the pelvic fascia, leva-

tor ani muscles and cervix, are most common. Less frequently it occurs anterior to the cervix. Congenital maldevelopment, defects, and variations in the pelvic floor are predisposing factors, and trauma at birth is the chief contributing cause.

The treatment is surgical, with abdominal perineal, or a combined approach, the second being preferable. The vaginal mucosa is incised longitudinally over the mass, the sac carefully dissected out, ligated and sutured behind the cervix. The pelvic floor is then closed by cross or purse-string sutures, after which the perineovaginal defects are corrected, excess vaginal tissue is trimmed off and the operative wound closed.²⁰

LEVATOR HERNIA

According to F C. Yeomans,²¹ a levator herma is one which extends through a rent in the levator ani muscle, it may be divided into a rare congenital type or a more usual acquired form and each group is subdivided into the perineal and pudendal form. The pudendal form may be anterior to the broad ligament (direct) or combined (indirect anterior)

The permeal herma presents in the ischiorectal fossa posterior to the transverus permei muscles. The boundaries of the internal ring are the broad ligament anteriorly, the uterosacral ligaments and rectum mesially in an imaginary line between the 2 sides of this angle. The sac is completely lined with peritoneum. The herma then perforates the rectovesical and ischiorectal fascia descending into the ischiorectal fossa.

Theanterior pudendal hernia is bounded at the internal ring by the uterus and bladder Mesially, the round ligament externally and the transversus perinei muscle and vagina below. The sac is incomplete, as the bladder, which forms the contents of the sac, has only a partial covering of peritonei. After perforating the rectovesical fascia, the posterior variety may pass downward and forward beneath the broad ligament before perforating the levator. The combined (indirect) variety is thus formed and it contains both bowel and bladder. The perineal and combined pudendal are always the sliding type of hernia.

The treatment of these hermas is high ligation of the sac and closure of the internal ring. The perineal herma usually presents no insurmountable difficulties of operative technic. If, as generally occurs, intimate adhesions to adjacent structures or to the perineal skin prevent excision of the sac, the internal ring may be closed by suture, or the sac may be obliterated by purse-string suture.

INTRA-ABDOMINAL HERNIA

Left Retromesocolic Hernia—Left retromesocolic hernia is about 3 times more frequent than the right. This type of hernia was described by Treitz (1857). In most of the cases, the hernial sac contained all the jejunum and most of the ileum. B. Halpert²² presented a necropsy case of left retromesocolic hernia, containing only a portion of the jejunum. He states, "This hernia, like the type which occurs on the right side, is to be interpreted as a malposition of the part of the small intestine involved, rather than as a herniation into a preformed peritoneal sac."

Hernia Through the Transverse Mesocolon and the Gastrocolic Omentum — Harold J Shelley²³ reports a case in which the entire small intestine from a posterior gastrojejunostomy and its component parts to within 4 inches

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of the ileocecal valve were herniated through an opening in the transverse mesocolon, across the lesser peritoneal sac and through an opening in the gastrocolic omentum. He was able to find only 2 similar cases reported in the lit-

omentum was explained by (1) excessive distention of the lesser sac with intestinal loops and spontaneous rupture of the gastrocolic omentum, or (2) operative opening of the gastrocolic omentum. The importance of properly sutur-

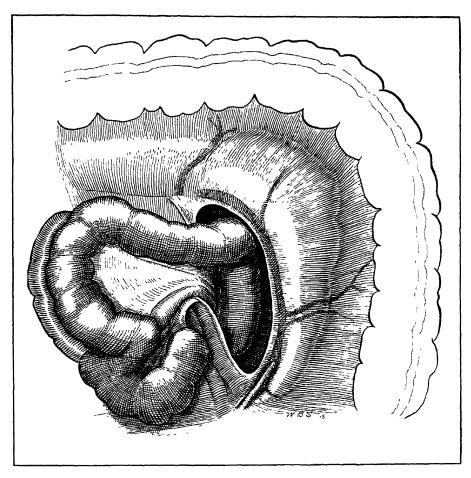


Fig 6—Below the transverse mesocolon, in the region of the duodenojejunal fossa, there is a peritoneal pocket which contains the left inframesocolic portion of the duodenum and from which 90 cm of jejunum have been removed. The anterior wall of the pocket containing the inferior mesenteric vein and the left colic artery in their usual relation is a part of the descending mesocolon, hence the name herma retromesocolica sinistia. (Halpert Surgery)

erature by Moymhan. This case was successfully treated by reduction of the hermated bowel, removing the gastro-jejunostomy, closing the openings in the stomach, jejunum, transverse mesocolon, and the gastrocolic omentum; and performing a Horsley pyloroplasty. The herniation of intestine across the lesser sac and through a hole in the gastrocolic

ing the edges of the transverse mesocolon to the stomach or stoma is emphasized by this case

MEDIASTINAL HERNIA

Mediastinal hernia is the protrusion of a portion of the contents of the pleural space of 1 hemithorax with evagination

of the mediastinal pleura through the mediastinal partition into the contralateral hemithorax. It is not to be confused with deviation of the mediastinum which is common in thoracic disease. It is not uncommon during the administration of pneumothorax H. C. Maier²⁴ reports 7 illustrative cases in detail, and presents typical roentgenograms of the 3 types of mediastinal hernia selected from a group of 30 cases in which pneumothorax was not present.

The structures of the mediastinum form an effective barrier between the 2 pleural spaces except for 3 weak places where only loose connective tissue separates the parietal pleural. One area hes directly behind the sternum, extends between the first and third ribs, and, occasionally, to the diaphragm Another weak place is between the aorta and the esophagus, extending between the levels of the fifth and eleventh thoracic verte-This type is less frequent than the former, tends to be smaller; and practically always extends from right to The third weak spot is between the esophagus and vertebrae, extending between the third and fifth thoracic vertebrae It is rare at this site.

The clinical significance of mediastinal hernias has in the fact that they may be confused with a pulmonary cavity. In empyemas which protrude through the mediastinum, the appearance may simulate that of a mediastinal abscess or even a bilateral empyema. In cases of pulmonary tuberculosis treated by thoracoplasty, herniated normal lung might be interpreted as being inadequately collapsed diseased lung on the thoracoplasty side.

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ANESTHESIA

By Henry S. Ruth, M.D.

SUBDURAL INJECTION OF ALCOHOL FOR RELIEF OF INTRACTABLE PAIN

The injection of alcohol into peripheral nerves for the relief of intractable pain has been performed many times during the last 10 to 15 years. The intradural injection of alcohol for pain was introduced into this country by Dogliotti in 1932. Since this time, this procedure has been found of definite value in various conditions where intractable pain is the prominent symptom.

Rationale-It is a well known fact that a larger amount of a local anesthetic is required to produce motor anesthesia than it does for a sensory block. There is evidence to prove that alcohol injected intradurally acts much in the same manner. It is, therefore, possible with the correct amount of alcohol to produce a sensory block without motor paralysis. The reasons given for this are: (a) The sensory nerves are smaller in size; and (b) they are less heavily myelinated than the motor nerves. The fact that the sensory roots are broader and less compact and thus expose a greater surface to the action of alcohol may also be a factor

Indications—The procedure may be worthy of a trial in any condition supplied by spinal nerves where severe pain is present to the degree that opiates are demanded. Most commonly it is indicated for inoperable carcinoma. It may also be of use in certain neuralgias, particularly sacrococcygeal neuralgia, caudalgia, and posthepatic neuralgia. It may be employed at times with excellent results for peripheral vascular diseases.

Site of Injection — The injection should be made at the point where the various pathways enter the spinal cord

by means of their respective spinal roots. Correction must be made for the anatomical facts that the dorsal roots are 1 spinous process above the corresponding interspace in the cervical region, 2 in the dorsal, and 3 in the lumbar region. Stern has mapped out the localization at which the injection should be made for all types of pain from the clavicle down. The second to third dorsal interspace should be injected for brachial plexus For angina pectoris, the patient should lie on the right side and the injection is made at the third to fourth dorsal region. For the upper abdomen, fifth to sixth or sixth to seventh dorsal interspaces; for the colon, the eleventh to twelfth dorsal, or the twelfth dorsal-first lumbar interspace. For lower abdominal and inguinal pain, the injection should be made between the eleventh and twelfth dorsal or between the twelfth dorsal and first lumbar. The second lumbar interspace should be employed for rectal pain.

Technic of Injection—It is preferable to employ an operating room table. The patient is placed in the usual lateral spinal position, with the painful side uppermost. It is believed the alcohol will affect 3 segments; the space at which it is injected, and 1 space above and 1 space below. Therefore, by means of breaking the table and producing lateral flexion of the spine, an attempt is made to have the interspace, at which the maximum degree of action is desired, the highest point of lateral curvature.

Preparation is then made as for an ordinary spinal anesthesia. After the tap has been made, 1 to 2 cc of spinal fluid may be drained off. The alcohol is then injected by means of a tuberculin syringe at a very slow rate. Injection should be

performed sufficiently slow so that the alcohol is placed drop by drop into the surrounding spinal fluid and when it is so placed, it is believed that it does not readily mix with the spinal fluid but rises to the highest level, namely, to the 3 dorsal roots which have already been selected by the patient's position on the table. Immediately after the injection, the same position of the patient should be maintained for at least 30 minutes. The only change in position which might be allowed should be a partial rolling so that the patient is slightly turned toward lying on his abdomen, in order that the posterior roots may receive the greatest action from the injected alcohol. It is customary to employ absolute alcohol, and preferably that which has been prepared in sterile ampoules in order to remove the hazard of spores. One cc 15 believed to be the maximum dosage for the dorsal region, while 0.5 to 0.8 cc is preferable in the lumbar region or below When injections are made in the upper dorsal region, great care should be emploved to see that the head is well below the level of injection, so that gravitational spread of alcohol does not take place toward the brain. After the injection, the patient should remain flat in bed for 24 hours

Immediately after the injection, or even in the midst of it, the patient's usual subjective symptom is that of a sense of warmth throughout the distribution of the nerves affected by the alcohol. It is advised that the injection be not attempted if paresthesias are produced during the spinal tap; such paresthesia denotes damage to a nerve. Likewise, if upon the injection of alcohol, the patient complains of a definite pain, the injection should be deferred. There may be a slight weakness of the upper portion of the leg if the upper lumbar nerves have been blocked, but if the above precau-

tions have been heeded, these will pass off within 2 or 3 days. It should be further noted that not more than 0.5 cc should be injected between the second and third lumbar vertebra, and not more than 10 minims below this point. Treatments by means of the subdural injection of alcohol may be repeated in 1 to 4 days

THE "POOR RISK" PATIENT AND SELECTION OF ANESTHETIC

"In anesthesia it is axiomatic that the drugs employed be chosen to suit the general condition as well as the surgical requirements of a given individual. This is equally true concerning the methods of their administration. Both become extremely important if the patient suffers some definite additional disability. It is well known that anesthetics are apt to disturb metabolism and to depress function. If these are already interfered with, the selection of the materials used and the modes by which they are given must be considered with the greatest care. While the desired and beneficial actions of anesthetics cannot be forgotten, the harmful effects may turn out to be manifold, indeed, all too often multiform "7

The following effects of anesthetics will be considered (a) In the blood; (b) on the liver, and (c) in the kidney

In the Blood—The 2 mam effects of anesthetics on the blood are, namely, effect on blood concentration and acidosis. It has been shown that ether anesthesia causes the blood solids to increase by 2 to 3½ per cent of the total weight of the blood. Since dehydration is often a feature in the handicapped patient, the selection of the anesthetic for that patient is an important decision. Preoperative intravenous injections of blood and isotonic solutions should be pre-

scribed, and the less toxic agents, nitrous oxide and cyclopropane, selected for the anesthetic agent.

It has long been recognized that acidosis is very likely to occur as a result of anesthesia. Acidosis becomes a serious matter for the handicapped patient, especially he who comes to operation already in a condition of acidosis, as, for example, the child with severe vomiting or the diabetic. Here it would seem that the choice lies between cyclopropane and spinal or local anesthesia.

On the Liver—Chloroform, even for short intervals, produces considerable impairment of the liver function Ether by inhalation also effects the function of the liver, proportionate to the degree and length of narcosis They return to normal, however, in about 48 hours, even after a 2-hour period of anesthesia Nitrous oxide and ethylene, when administered without any oxygen deprivation, do not show either immediate or delayed impairment of hepatic function. When the percentages of oxygen are reduced during their administration, an impairment of function has been shown to take place which does not return to normal as quickly as with impairment following Liver function is not ether anesthesia disordered following the anesthesia produced by barbituric acid derivatives, by avertin, by vinyl ether, and absolutely not at all, by cyclopropane

In the Kidney—It may be said that all general anesthetics cause some depression of kidney activity, wherein the rate of secretion and composition of the urine is lowered. The degree of depression varies directly with the depth of narcosis and the effects are influenced by the condition of the kidneys, by the water content of the blood, and by the duration of anesthesia. With these factors in mind, it is evident that in surgical procedures on patients handicapped by kidney dis-

ease, both the selection and the administration of anesthetics become of grave consequence.

Selection of Anesthetic—The above considerations are more important, of course, with the poor risk patient. This class of patient is excellently described by Sise8 as "one whose chances of death or morbidity following operation are decidedly greater than those of the average individual. The factor which is most important in making a patient a poor or dangerous risk is usually his general vigor. This factor is, unfortunately, somewhat intangible and difficult to determine except by 'hind-sight,' but is none the less of the greatest importance. In some patients, this intangible quality is of such strength that it carries the patient through all dangers, while in others it is so feeble that they may succumb quite easily."

"With poor risk patients there is, then, more reason even than usual for selecting an anesthetic which is safe and as little upsetting to the patient as possible. The various anesthetics may be listed roughly as follows, in the order of their desirability from this standpoint, although under the various conditions of their clinical application there would undoubtedly be many changes in this order.

"The local-acting anesthetic drugs, including low spinal anesthesia

"Combinations of general anesthetics, sometimes with local-acting drugs in addition

- "Inhalation anesthetics
- "Intravenous anesthetics
- "Rectal anesthetics
- "High spinal anesthesia

"The local-acting drugs are, on the whole and with some well-marked exceptions, the safest and least upsetting, and therefore, with a poor risk patient, should be first choice whenever they

are effective for the proposed operation, in that they enable the operator to do his work safely and thoroughly unhampered by inadequacy of anesthesia, and in that the patient is comfortable. All too frequently, however, they fail in one or the other, or both of these respects. All too frequently, also, they fail or even are not tried because of the limitations of the anesthetist or surgeon.

"Various procedures of regional anesthesia are not entirely without dangers In caudal anesthesia, the region injected is very vascular and is near the dural sac, so that the inexperienced anesthetist may easily make an intravenous or subarachnoid injection. Even if this is not done, the combination of a vascular region and a cavity which is incompressible in most directions makes the possibility of rapid absorption quite marked Marked depression sometimes occurs and some deaths have taken place

"Spinal anesthesia varies greatly in danger according to a number of different factors, such as the competence of the anesthetist with this particular form of anesthesia, the height of anesthesia, length of operation and condition of the patient" A low spinal anesthesia, one below the abdomen, is quite safe and often very desirable for operations in this region ... especially if the duration of operation is not great. It is quite a different matter, however, when the level of the anesthesia begins to reach into the abdomen, even to the limited extent necessary for suprapulae operations on the bladder. Here depressive effects begin to manifest themselves, and, when the entire abdomen is anesthetized, they may be quite marked. The beneficial effects of this anesthesia are probably more marked in the abdominal region than in any other part of the body. . . . In fact, so outstanding are these benefits that the decrease in danger of the operation often overbalances the increase in danger of the anesthetic so that the entire procedure of anesthesia and surgery becomes less dangerous for spinal anesthesia than with some other type of anesthesia."

"There are many combinations of anesthetics that are often most useful Their basis is usually one of the gases with ether. These may be preceded by administration of avertin, a barbiturate. or paraldehyde as a basal anesthetic, and local anesthesia or field block, the latter especially in abdominal surgery, may be added. Nitrous oxide-ether is a popular and useful combination. The fact that it is usually explosive, however, does not seem to be fully appreciated When but a light anesthesia is needed, we prefer nitrous oxide-cyclopropane With these combinations, depth of anesthesia can be obtained more safely than with any one of their constituent anesthetics alone. This is because the toxic effects, being often different in character, are not so cumulative as are the anesthetic effects. which are at least very similar Various combinations may be used for a wide variety of procedures, since they are extremely flexible By varying the anesthetics and their proportions, almost any type of anesthesia may be obtained ... They are widely used by large numbers of anesthetists and their safety and efficiency depend largely on the judgment and skill with which the proportions of the various drugs are adjusted to the operation and to each other. They are usually inflammable and explosive and should, therefore, not be used in the presence of roentgen rays or diathermy It should be remembered that more explosions have taken place with nitrous oxide-ether mixtures than with ethylene or cyclopropane. On the whole, these combinations should be given a high place in safety, efficiency, and general usefulness.

"The gases, when used alone, are rated as less safe, and therefore less suitable for poor risk patients than are the combinations. With pure nitrous oxide-oxygen in particular, some degree of anoxemia is almost sure to be present, and this complication is very bad for these patients, and may, indeed be quite dangerous. Ethylene is, in some ways, one of our best inhalation anesthetics because it has little or no toxic action on any of the organs or functions of the body and because less anoxemia occurs with its use than is the case with nitrous oxide . . . Cyclopropane . . has a distinct toxic action which shows itself in irritability of the heart with irregular action during (deep) anesthesia and in postoperative vomiting, general upset, and sometimes in marked postoperative drop in blood pressure. All these signs of toxicity are much more marked when the higher concentrations are employed When but a light plane of anesthesia is used, there is hardly any evidence of them, and under these circumstances it forms a safe and useful anesthetic

"Ether also is a drug whose toxic action varies widely according to the depth of anesthesia employed At considerable depth, as frequently employed, it has well-marked toxic action. There is postoperative depression, nausea and vomiting, upset of the acid-base balance, interference with the metabolism of sugar, and lowering of the function of the liver and kidneys During operation it increased the susceptibility to shock, but is otherwise quite safe in its immediate effects If, however, but a very light plane of anesthesia is maintained, 1 of these toxic effects is usually manifest .

"Vinyl ether is too toxic a drug to be suitable for use with these patients except for brief administration . . . The fact that it is highly portable may make it more useful under some circumstances than the gases.

"Ethyl chloride can be used in a similar manner, but is so much less safe than vinyl ether that the latter should be preferred . . .

"The intravenous and rectal anesthetics have the advantage that they are free from danger of fire and explosion, but that, unlike pure nitrous oxideoxygen, their use is not accompanied by anoxemia. They are, therefore, often preferable to nitrous oxide for a light anesthetic in the presence of a source of ignition, since these patients are easily injured by anoxemia. Since these anesthetics are ordinarily followed by less nausea and vomiting than are the inhalation anesthetics, they are occasionally useful with patients who have shown unusual tendency to postoperative vomiting.

"With intravenous anesthetics, control of anesthesia, that is, the rapidity with which it may be lightened, is fairly good, approximating that with ether, but with rectal anesthetics control is so poor that they should not be used for more than basal anesthesia. However, control of intravenous anesthesia may be greatly slowed in the presence of shock, and this method should not be used, therefore, when this is likely to supervene Since these drugs are detoxified in the liver they should not be used when there is marked lowering of the function of this organ, and since they are excreted by the kidneys they should probably not be used when there is marked functional renal incapacity. They should not be used in patients with extreme feebleness because depressive effects, especially on respiration, are sometimes marked Like some other anesthetics, notably pure nitrous oxide-oxygen and spinal anes-

thesia, they may, if not correctly given, be quite dangerous....

"The chief influence exerted by poor condition of the patient in relation to site of operation is in the abdominal region, where spinal anesthesia may be desirable. Here a nice judgment of various opposing factors is often required. It is obvious that high spinal anesthesia may be quite dangerous for a patient in poor condition. On the other hand, this anesthesia will make operation safer, and will lessen postoperative upset. If the operation is short, and the dose of the drug is small, it will be safer than otherwise, and if the operation is of technical difficulty, it will be more urgently needed than otherwise That even a long operation in the upper part of the abdomen does not absolutely contraindicate the use of spinal anesthesia in a patient in poor condition, if the operation is one of special technical difficulty, is shown by our experience with resection of the stomach, where spinal anesthesia, with 1.1500 nupercaine solution has proved to be on the whole the most successful anesthetic.

"If the difficulty which renders a patient a poor risk is damage to some one of the vital organs, this should influence the choice of the anesthetic considerably Valvular disease of the heart does not influence greatly the choice of an anesthetic in the absence of impending or actual cardiac failure Cardiac failure, however, or myocardial disease, greatly increases the danger. Here the more toxic inhalation anesthetics should be avoided, especially in high concentration Cyclopropane, in high concentration, has distinct possibilities of danger, although there is as yet no real consensus of opinion on this point A low concentration may actually be of value because of the high content of oxygen which may be used Ether is not so harmful, and while high concentrations are undesirable, the use of low concentrations for a light plane of anesthesia is well adapted to these patients. Since anoxemia is harmful, pure nitrous oxide-oxygen, especially when pushed to considerable depth, may be dangerous. Marked changes of blood pressure either up, as with cyclopropane. or down as with spinal anesthesia, are undesirable especially with coronary disease. On the whole, and with some exceptions, patients with serious heart disease are most safely operated upon under regional anesthesia when it is applicable, not forgetting that simple nervousness may be a decided contraindication with these patients; under spinal anesthesia in operations below the diaphragm, and under a combination of anesthetics or light ether anesthesia in other conditions

"In cases of marked damage to the liver, the toxic drugs in high concentration should also be avoided. Here the positions of cyclopropane and ether are reversed, since cyclopropane appears to be quite innocuous, while it is ether that is more harmful . Anoxemia is quite harmful to the liver and markedly intensifies any harmful effects of the anesthetic drugs and should be studiously avoided at all times. The influence of renal damage is similar to that of hepatic The same drugs should be damage avoided .

"Although operation had best be avoided in the presence of disease of the lungs, such as bronchitis or pneumonia, it is, unfortunately, sometimes necessary. In these circumstances it would seem from theoretical considerations that ether would be very bad, and this belief has given rise to the term 'ether pneumonia' in cases in which pneumonia has followed operation under this anesthetic. Curiously enough, however, the anesthetic used has little effect on the inci-

dence of postoperative pneumonia or on lung pathology when this is already present before operation. The use of local anesthesia offers no assurance of freedom from these complications, nor does the use of ether by any means guarantee them. The main influences on lung conditions appear to be elsewhere than in the anesthetic. One careful investigator has, indeed, gone so far as to suggest that ether, so far from being injurious, actually may have a favorable The avoidance of complicaınfluence tions and exacerbations in the presence of lung pathology appears, then, to lie not so much in the actual decision concerning which particular anesthetic drug shall be used, but rather in the site of operation, and in all measures which maintain the resistance of the patient, such as warmth, the reduction of operating time to the minimum, the method and skill with which the anesthetic is given, and the avoidance of high concentrations of toxic drugs, just as with any other patient in poor condition."

PRESENT STATUS OF THE BARBITURATES

In a most outstanding article, Tatum⁹ has adopted "the primary objective of furnishing leads to various aspects of the barbiturate problem as well as to supply useful information"

Brain—"The bram is the chief site of action in that hypnosis and annesia, and in overdosage, anesthesia and coma, are the commonly expected dominant effects". He points out the evidence that the barbiturates apparently act predominantly upon the basal ganglia and hypothalamus.

Respiration—"Barbiturates cause a depression of the respiratory center, the activity of which, however, may be main-

tained by oxygen want operating upon and through the sino-aortic mechanism. Free oxygen supply, by diminishing oxygen want, may cause the appearance of greater depression. Thus barbiturates appear to depress the central respiratory center mechanisms more than the sinoaortic mechanism."

Circulation—1. Vagus—Up to the present time it appears that the barbiturates are depressants to the cardiac vagus mechanisms of animals and that this depression occurs in the peripheral vagal ganglia. In ordinary doses, it appears that barbital and phenobarbital do not effect the vagus, whereas others, such as amytal, pentobarbital and pernoston are effective in this depression in moderate doses.

2 **Heart**—The only cardiac effects of anesthetic doses of barbiturates, other than thiobarbiturates, as shown by the electrocardiogram, appear to be an increase in heart rate and a decrease in the common sinus arrhythmia seen in dogs and cats.

It is obvious that the question of cardiac irregularities ascribed by some sources is still open to question and still may be seen occasionally in laboratory animals under the influence of thiobar-Other factors must be seribiturates ously considered before one is justified in ascribing irregularities to any one etiological factor, particularly to new drugs To date, therefore, the information offered by some investigators that the thiobarbiturates have not been proven to produce irregularities appear to have the best of the argument, and until further observations to the contrary have been made, one must conclude that in man, at any rate, no significant alterations in heart action can be ascribed to the specific activity of either barbiturates or their thio-derivatives

3. Vasomotor Mechanism—Varying degrees of depressing action on the carotid sinus have been reported with the various barbiturates. "Thus, we have further evidence relative to the different potentialities of the different barbiturates in their modification of activity of peripheral mechanisms. Both the vagus in its peripheral cardiac action and the sinoaortic mechanism in its reflex action are modified differently by different members of the series."

4 Blood Vessels—Barbiturates, generally speaking, produce a fall in blood pressure, and the fall in degree is related to the speed of injection; the more rapid the injection the greater the fall in blood pressure "Marx has called attention to the increased permeability of blood vessels, which may be a factor in causation of cerebral edema so often seen in serious human poisonings by these drugs. The drop in blood pressure is obviously due to vasodilatation"

Spinal Cord-Some of the barbiturates, such as evipal, amytal, barbital, and luminal show a "markedly raised threshold of flexion reflexes. Lowering of the threshold by strychime can be effectively overcome by barbiturates, even to the extent of practical elimination of all crossed reflexes."

Smooth Muscle—It appears that barbiturates in any effective concentration produce "a depression of intestinal, uterine and ureteral muscle in vitro" "Any stimulant action in vitro due to alkalinity of strong solutions is overbalanced by the depressant action of the drugs" Burstein has "called attention to this primary depressant action of short-acting barbiturates in vivo followed by a prolonged increase in contractions and tonus." In addition, barbiturates "depress the urinary bladder stretch reflexes of the cat," depress the "irritability and peristaltic activity of ureters in vitro," and it seems

that relatively strong solutions are necessary to depress both pregnant and non-pregnant uteri of rabbits. The presence of barbiturates has been demonstrated in the fetus.

Kidney Action—"Any suppression of urinary activity during the short periods of anesthesia was entirely compensated for by a subsequent and transient period of increased action. The kidney function is thus not seriously affected, provided the period of deep depression is not long."

Blood—"In general, the constitution of blood is relatively little affected by the barbiturates when given in moderate dosages" "It is generally held that the blood sugar is not changed significantly by barbiturates unless depression reached such a grade as to bring on acidosis."

Metabolism — From evidences reviewed, "we are forced to believe that apparent discrepancies between different observers are simply due to differences in dosage and that, in light hypnotic doses, no significant depression below the resting stage occurs, whereas if a more profound depression occurs, a fall in basal metabolic rate is entirely in line with expectations"

Elimination and Detoxication — "In usual therapeutic dosages, barbiturates are, for the most part, destroyed in the body of mammals and only barbital and luminal appear consistently in the urme" Any "dangerously large doses of most of the barbiturates will appear in the urine; hence it is likely that there exists a renal threshold for the barbiturates" It has been shown that "in instances of injury to the liver, for example, by chloroform or carbon tetrachloride, the short-acting or more unstable barbiturates become longer acting. These conclusions were essentially confirmed" by others who "observed that double nephrectomy had little or no effect

on the duration of short-acting barbiturates, whereas barbital depression was continued until terminus due to the consequence of nephrectomy." "The problem of possible changes in the rate of destruction according to conditional states has yet to be answered except in instances of parenchymatous damage such as are effected by chloroform or other poisons which particularly affect the liver."

Synergism — It has been generally conceded that when the barbiturates are employed before the use of a general anesthetic, the amount of the general anesthetic necessary as well as the concentration required for complete anesthesia and relaxation are markedly reduced. A similar synergism appears to exist through "the well-known potentiation of barbiturates by morphine."

Antagonism—"Maloney et al. called attention to the superior efficacy of picrotoxin as a stimulating analeptic." "Coramine as well as caffeine is capable of arousal or partial arousal in animals not profoundly depressed. In the case of deep depression these agents are followed by added depression, and hence are not appropriate to the antagonism in question if recovery is expected. Metrazol has its advocates and comes close to picrotoxin in lifesaving capacity, and somewhat like picrotoxin, appears to stimulate much the same centers vitally concerned in profound barbiturate depression" Strychnine can not be expected to be of much value

"The converse situation is rather different." "Strychnine, cocaine, procaine, metrazol, picrotoxin, thujone, insulin in excess, etc, all are effectively controllable within certain ranges of dosages by symptomatic administration of barbiturates" "By and large, barbiturates appear to be surprisingly effective in controlling convulsions of most organs

in that they appear to be selectively depressant on centers or pathways involved in the convulsive processes with, at the same time, less direct action on centers controlling respiration and vasomotor activity." "The barbiturates appear to be functionally decerebrate without at the same time seriously impairing vital medullary centers. The anesthetics, on the other hand, appear equally capable of blocking out convulsive processes, yet they seem to be so much less specific in action that the vital centers are apt to be simultaneously depressed even to the stage of paralysis."

Classification — Werner, Pratt and Tatum classify the barbiturates as follows: Barbital and phenobarbital are represented as long-acting; neonal and dial as intermediate, amytal and nembutal as short-acting, and finally, evipal and pentothal as ultra-short-acting barbiturates. "While there are members occupying a borderline status and hence not readily placed, the idea as a whole permits the rational selection of one or other of the ever-increasing series, according to experimental and clinical needs" "It so happens that with the exception of barbital and phenobarbital, practically all of them have a short induction period and hence this basis of classification scarcely suffices to be of significant and practical value"

Toxicology—"The etiology of porsoning is for the most part self-medication. In many cases, perhaps the greater proportion, the poisoning is intended suicide; others develop a psychic dependence, and hence take the drugs in too large dosages, long after need has ceased, and develop chronic poisoning; finally, there is that peculiar condition spoken of as 'automatism' by Richards. In this condition the individual, having become accustomed to the use of the drugs, may at some time fail to have

deep sleep develop. In this twilight zone, an individual does not exert normal inhibition and reason, and hence mechanically takes all the remaining tablets or capsules. In these cases the coroner's jury pronounces the cause of death as suicide, and so it is, but it should be recognized scientifically as unintentional or accidental suicide recognition of this possibility by the medical and pharmaceutical professions might well effect a reduction in the number of accidents of this nature Diagnosis of poisoning depends upon history, circumstantial evidence, and finally on chemical analysis of excreta, gastric contents, or tissues and body fluids"

Habituation—"Repeated and continued use of barbiturates induces a condition of habituation or psychic dependence but apparently not a true addiction as exemplified by use of morphine and herom"

Treatment of Acute Poisoning -From a review of many reports it is clearly apparent that from the work of clinical investigators, they are convinced that *picrotoxin* is the most effective and sustaining analeptic for clinical barbiturate poisoning "It is safe to anticipate that those who are familiar with the evident potency of picrotoxin, properly administered, would elect to use it in serious cases of barbiturate poisoning since a small dosage of a potent drug will work in mild cases, and larger doses may work in serious cases, whereas weak analeptics will likely fail except in instances of minor and nonserious poisoning"

Clinical Indications—1 Hypnotic. "Since these drugs are not analgesic except in overwhelming dosages, pain as a cause of insomnia requires other therapy. The choice of hypnotic must depend upon circumstances, such as the possibility that if sleep once is started it will

continue more or less normally For this purpose a short-acting drug would obviously be desirable "As a general rule, the short-acting barbiturates are freer from after-effects, such as mild depression" "If a more or less continuous depression is required through both day and night, a drug such as phenobarbital in repeated small doses very often gives satisfactory results. This is accomplished in epilepsy and in hyperirritability of elderly people"

- 2 Preanesthetic Depressant. "Many surgeons and anesthetists have found that the use of appropriate barbiturates may be satisfactorily employed to quiet a patient prior to anesthesia induction and thereby diminishing 'psychic trauma'."
- 3 Anesthetic "The consensus of most students of anesthesia is that the barbiturates, with 2 exceptions, do not meet the requirements of anesthetic agents, particularly in regard to analgesia and to possibility of moment to moment control. The 2 exceptions that may be said to meet 1 of these requirements fairly closely are evipal and pentothal."
- 4 Anticonvulsant —"\gamst convulsions of cerebral origin barbiturates have been found to be of particularly specific efficiency, as for example against cocaine, thujone, metrazol and picrotoxin, and less specific and satisfactory against cord convulsants such as strychnine" "In all instances the control of convulsions should be by careful symptomatic administration of an antagonistic drug. The severity of convulsions scarcely suffices to indicate the amount of drug to be given."

Neuropsychiatry — Barbiturates are still being employed for this application and "the current practice is to provide the patient with a prolonged and enforced mental rest whereby the habit of CANCER 849

psychotic activity may be broken through inactivity

"The use of phenobarbital in treatment of epilepsy appears to depend upon a long continued but mild cortical depression and is still, generally speaking, the drug of choice, though 'dilantin,' a non-hypnotic drug, has effected a peculiar and unanticipated controlling action. It is thus possible that a better understanding, of idiopathic epilepsy may be obtained through this interesting, though not entirely safe, hydantoin derivative."

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CANCER

By Clark E. Brown, M D.

Etiology—B. Lucké¹ has established the final proof of the malignancy of renal adenocarcinoma in the leopard frog, demonstrating that metastases from the kidney occurred in the liver, pancreas, intestines, peritoneum, etc., presumably by the blood stream Transplantability of the tumor was finally demonstrated by Lucké and Schlumberger² when they secured 53 per cent takes in the anterior chamber of the eye Here they observed the tumor growth characteristics through the slit-lamp microscope. Two interesting conclusions arose from their observations, namely that these cancers appear to be much more responsive to laws governing growth and organization than was commonly supposed, and that the structure of the tissue invaded determines to an extent the character of the growth These experiments on cancers in cold-blooded animals are particularly timely with reference to the recent work on the destructive action of cold on malignant tumors in humans

Much speculation has taken place in recent years as to the carcinogenic activity of the estrogens. This subject is particularly important because of the extensive use of the various estrogens in endocrinology. W. U. Gardner³ has reviewed the rôle of estrogens in carcinogenesis. He brings out the fact that in certain strains of mice intrinsic factors such as heredity are more important than the estrogens in producing carcinoma of the breast, while in other strains the intrinsic factors may be dominated by the estrogens especially when estrogens are administered over long periods. Even in low tumor strains a few breast carcinomas have resulted from the prolonged administration of an estrogen As regards the estrogens themselves, their influence in producing mammary adenocarcinoma seems proportional to their physiologic activity. The author points out the particular significance of the development in these animals of uterine carcinoma. The spontaneous incidence of uterine cancer is very low in mice In the development of uterine cancer the glands go through the preliminary proliferative phase seen as the usual endometrial response to an estrogenic hormone It becomes evident there-

fore that in these animals the cancers occur in organs in which the estrogens produce continued and repeated growth processes. Numerous other neoplastic processes have developed in animals under continued estrogenic stimulation. Among these are benign uterine fibromas in guinea pigs and sarcomas of the soft tissues as well as lymphatic leukemia in mice. The author does not pretend to draw any inferences between the animal work and prolonged estrogen administration in humans He quotes Cramer,4 however, as stating that "therapy extended over several years . . . does involve such a risk especially in susceptible individuals, that is to say in women with a family history of mammary cancer "

One of the commoner clinical observations on the etiology of cancer has been the comparatively high incidence of skin cancer in nonpigmented peoples residing in the tropics as compared with those less exposed to prolonged sunlight. In 1935 Roffo substantiated this observation in albino rats. II. P. Rusch and C A Baumann⁵ have produced skin cancers in over 50 per cent of a large series of white mice exposed to the ultraviolet light from a quartz mercury vapor lamp Various transitions through papillomas were produced before the development of invasive squamous cell carcinomas. Mice receiving daily exposures of from 30 to 60 minutes developed ear tumors in 31/2 to 9 months Mice receiving the longer daily exposures developed tumors more rapidly. An extremely interesting feature in the work was the failure of high incidence strains of manimary carcinoma white mice to develop more tumors than the low incidence Strains of dark-haired mice showed a smaller tumor incidence than the white mice

Ever since the clinical use of thorium dioxide for diagnosis, there has been speculation as to whether this radioactive substance is carcinogenic Sarcomas have been produced in rats and carcinomas in mice by the local action of thorium dioxide over long periods. This year L. Foulds⁶ succeeded in producing 1 carcinoma and 3 sarcomas in guinea pigs by 4 injections of 02 to 03 cc. quantities of undiluted thorotrast into the mammary glands of female guinea pigs. Three years was required for the development of these tumors. The breast carcinoma was of the mammary alveolar type and this with 2 of the sarcomas was successfully transplanted. The unusual feature in this work is the fact that guinea pigs are particularly refractory to the development of spontaneous tumors or tumors from carcinogenic agents. No skin cancers have been reported from tar or carcinogenic hydrocarbon applications, and only 21 spontaneous cancers have been observed Sarcomas have been produced in guinea pigs by the subcutaneous injections of benzpyrene Radium implants have also produced malignant tumors of connective tissue as well as of epithelial origin in these animals

Certainly one of the least expected sites for the development of tumors from extrinsic stimulation is the brain. And vet A. M. Seligman and M. J. Shear⁷ have produced both gliomas and meningeal sarcomas in mice by the intracerebral injection of pellets of 20-methylcholanthrene Of a total of 20 mice so injected, 11 developed gliomas and 2 meningeal sarcomas Dr. Leo Alexander after study of the material stained differentially, classified 2 as spongioblastoma multiforme, I as oligodendroglioma, 1 as pinealoma, 3 as spongroblastoma polare, 1 as ependymoma, 2 as neuroepithelioma, and 1 as fibrillary astroCANCER 851

cytoma. It is interesting to note that all types of glial tumors except the medullo-blastoma developed in response to carcinogenic hydrocarbon stimulation. The absence of medulloblastoma might be explained by the fact that the cerebellum was not injected.

A possible pathogenesis for the development of dermoid tumors has been suggested by the experiments of S. P. Reimann and B. J. Miller⁸ on unfertilized human ova. Five such ova were obtained from human fallopian tubes removed on the fifteenth and sixteenth days after the onset of the last menstrual period. In 1 ova by suitable mechanical stimulation (a needle prick) there was produced extrusion of polar bodies thereby initiating a phase of 1 type of segmentation The authors consider this as evidence of parthenogenetic activity of the human ovum, and suggest that dermoid cysts and teratomas may develop in situ as a result of parthenogenetic glowth of such ova

Bone Sarcoma—F. Parker, Jr, and H Jackson, Jr, 9 have recently described a type of bone sarcoma hitherto unrecognized. They have collected and reclassified from their own material and from the Registry of Bone Sarcoma 17 cases designated as primary reticulum cell sarconna of bone which had previously been grouped under various headings such as Ewing's sarcoma, Hodgkin's disease, lymphosarcoma, osteogenic sarcoma. 1eu kosarcoma and inflammation These tumors differ from the above types with which they were previously classified both clinically and pathologically. They begin in the medullary portion of long bones usually, destroy the cortex, and extending into the soft tissues sometimes produce relatively bulky masses there. The patient's general condition, in spite of the extensive local pathology, frequently remains unusually

good. Metastases occur late and frequently involve the regional nodes or amputation stump. The tumor is composed of reticulum cells with clear cytoplasm and large nuclei indistinguishable from those composing primary reticulum cell sarcoma of lymph nodes. By suitable staining methods reticulum fibers can be shown to be intimately associated with the tumor cells. But where reticulum cell sarcoma of lymph nodes is usually fatal in 3 years, this primary tumor of bone pursues a much more benign course. Thirteen of the 17 cases were alive from 6 months to 14 years after the initial symptoms of the tumor. Seven of these patients were free from disease 10 years after treatment. The treatment of choice is immediate amputation and radiation.

Radiation alone has produced no 5-year cures. It is highly important that this group of primary bone sarcomas has been segregated because their classification in other groups has undoubtedly raised the percentage cures of those types of more malignant bone tumors. Some credit is due the Registry of Bone Sarcomas, I believe, for its efforts in assembling a large volume of material of this kind for study. Undoubtedly further valuable investigative work will come from the various tumor registries now in existence.

Hydatidiform Mole and Chorion-epithelioma—A. Mathieu¹⁰ has made a comprehensive review of the literature on hydatidiform mole and chorionepithelioma of the past 3 years. The study includes 576 cases of mole and 266 cases of chorionepithelioma. The mortality rate of these two types of chorionic tumors was 2 per cent and 10 per cent respectively. This obvious reduction in mortality below previous periods is due undoubtedly to the widespread use of the Aschheim-Zondek test in diagnosis of

the early clinically suspicious cases. Aschheim demonstrated nearly 10 years ago that the gonadotropic hormone was present in the urine of these patients in concentrations higher than those usually found in pregnancy In rare instances the author encountered reports in which the gonadotrophic hormone in the urine of patients in the second month of pregnancy reached the high titer exhibited by patients with mole or chorionepithelioma Also rare reports were encountered in which the hormone excretion of patients with these intrauterine tumors did not exceed the level of between 100,-000 and 200,000 mouse units per liter considered by some to be the minimum The quantitative assay of the hormone in patients suspected of having mole or chorionepithelioma, however, is by far the most valuable diagnostic and prognostic test available today.

In considering its application to determine the presence of postoperative recurrence, it should be remembered that lutem cysts arising coincidently with these tumors may persist to give a high gonadotrophic hormone excretion for as long as 8 weeks following complete removal of the uterine tumors. The hormone excretion is increased for only about a week following the termination of a normal pregnancy. The author emphasizes the impossibility of the majority of the profession to secure the quantitative Aschheim-Zondek or Friedman tests in suspected cases of hydatidiform mole or chorionepithelioma. He gives 10 suggestions to bear in mind in interpreting and applying the qualitative tests for the detection of these tumors. I quote a few of the more important ones. "Absolute reliance should not be placed on any 1 test and in questionable cases the test should be rechecked and rechecked. The spinal fluid gives a negative test in normal pregnancy and a positive test with mole or chorionepithelioma. The biological test should overrule contrary clinical and pathological findings."

Malignancy in Childhood—Cancer in children is a relatively rare disease. H W Dargeon¹¹ abstracted the following statistics from the New York City Department of Health:

Death from Certain Causes 0 to 14 Years of Age

Year	All Causes	Carcinoma
1934	8403	51
1935	. 8090	70
1936	7163	54

Sarcomas far outnumber the carcinomas in childhood Malignant tumors in this span of life have a greater tendency to rapid growth and early metastasis Embryonic and neurogenic tumors have a greater proportional incidence in childhood, the commoner of the embryonal variety being teratomas and mixed tumors (adenosarcoma of Wilms). and the commoner neurogenic tumors including neuroblastomas and retinal gliomas During the 8 years following 1930 the author states that 200 cases of childhood cancer were noted in the Memorial Hospital Only 23 of these were carcinomas and 33 were lymphoid malignancies. The 3 commonest sites for this group of malignancies were the bones (79), soft somatic tissue (41) and the head and neck (37). A combined review of the literature gave the following most frequent topographical distributions for childhood cancers: (1) Central nervous system; (2) bone, (3) eye (retinal glioma), (4) genitourinary, and (5) lymphoid system

B. L Coley and R. L Peterson¹² have reviewed the commonest types of bone tumors in childhood They list persistant pain in an extremity as the most important symptom. The pain is at first transient, usually worse at night It may

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precede the swelling by weeks and months. Osteogenic sarcoma usually begins in the metaphyseal region, endothelioma (Ewing's tumor) in the diaphysis. giant-cell tumor in cancellous bone near the articulation, and bone cysts on the shaft side of the epiphyseal line If an extremity swelling appears just after a muscle bruise, grows rapidly at first then soon reaches a quiescent stage, the authors suspect myositis ossificans. Stereoscopic views are essential to the diagnosis of bone tumors If no bone pathology is seen by x-rays, sarcoma can be ruled out. Amputation or prolonged irradiation should not be carried out unless microscopic confirmation of clinical and radiologic data is obtained. In treating osteogenic sarcomas the authors favor a short intensive course of preoperative irradiation before amputation This tumor is radioresistant. Postoperative administration of Coley toxin may diminish the chances of pulmonary metastasis.

Ewing's sarcoma is proportionately common in childhood, 95 per cent of a series of 65 cases occurring under 25 years This tumor commonly masquerades as subacute or chronic osteomyelitis in children and is frequently associated with fever, leukocytosis, tenderness and fusiform swelling. Aspiration biopsies are especially useful in the diagnosis of these tumors Ewing's tumor appears radiosensitive, but radiation is followed sooner or later by recurrence or metastasis. Adequate irradiation followed by amputation is the method of choice Chondromas are fairly common childhood tumors Although less than 10 per cent of them becomes malignant, they should be removed as a precaution. The authors have encountered 6 cases of liposarcoma of bone Preliminary radiation followed by amputation is advisable Laboratory data should include in all cases of bone tumor a Wassermann examination, serum phosphatase, complete blood count, and a study of the urine for Bence-Jones' protein.

H. E. Martin¹³ states that practically every anatomic form of cancer occurring in adults may be found in children. In adults, however, the lesions occur at sites of chronic irritation, such as the skin of the face, the lower lip, the anterior twothirds of the tongue and the mucosa of the cheeks. In children this topographical relation to irritation is not maintained The spontaneous cancers of children are of a higher degree of malignancy. In 7 years at the Memorial Hospital 44 malignancies in children occurred in the head and neck. The commonest type of malignancy in this site was the retinal glioma (14 cases). This tumor is believed to be congenital. The pupil of the affected eye becomes fixed, dilated, and gives a so-called white reflex Twentyfive per cent of the cases are bilateral. If unilateral, the treatment is enucleation. Generalized metastases frequently occur. Carcinomas of the pharynx and palate are occasionally encountered (7 of the 44 cases) These growths are generally very anaplastic and are highly malignant The authors never excise a cervical node for biopsy without an exhaustive search of the upper respiratory and alimentary tracts for a primary focus Fortunately, the commonest cause of enlarged cervical nodes in children is benign inflammation Carcinoma of the skin accounted for 5 of the 44 malignancies in the head and neck Both squamous and basal cell types were noted

Benign congenital tumors of a vascular nature are relatively common in child-hood and infancy W. L. Watson¹⁴ details the treatment of the more frequently encountered forms of hemangioma and lymphangioma. The capillary hemangioma or port wine stain exhibits a poor response to x-rays. It usually responds

well to any of 3 methods and the selection depends upon the size and location of the affection. The 3 methods are:
(1) Blistering doses of ultraviolet irradiation; (2) application of carbon dioxide snow for 15 or 20 seconds, and (3) surgical excision and skin grafting.

Cavernous hemangiomas are radiosensitive In addition to radiation, surgery. and sclerosing injection compounds may be used. Radium applications in small dosage are efficacious, or gold radon implants and possibly low voltage x-rays. Excision may be satisfactory if the hemangioma is located where scarring will not produce deformity Five per cent sodium morrhuate injections have been tried in 104 cases of cavernous hemangioma with good results Simple capillary lymphangiomas are radioresistant, while the cavernous lymphangiomas are fairly radiosensitive Cystic lymphangiomas of the neck or hygromas carry a high operative mortality mortality in these tumors results largely from infection and reaches 43 per cent in the series quoted by the author Sodium morrhuate has been used successfully in 1 case. In a series of 29 cases reviewed recently by R E Gross and C F Goeringer, 15 2 patients died as a result of operation Both died of infection, but in 1 the cyst was infected prior to operation These authors object to the injection method because of the possible connections of the hygromas to important veins in the neck.

the proportion of ultimate metastases (Wood, Flexner and Jobling). year R Paterson and J. R. Nuttall16 completed a clinical experiment designed to demonstrate that biopsy of squamous carcinomas in humans did not increase the number of subsequent lymphatic or vascular metastases. They chose a group of superficial lesions of the skin and mucous membranes of the mouth for the following reasons: Malignant lesions in this site could be fairly well recognized grossly and metastases to the cervical nodes become evident readily if they occurred. These lesions respond well to surface irradiation so that the study was not complicated by the incidental trauma of surgical removal or interstitial implantations. Only squamous cell cancers were included in the biopsy group. Ulcerated lesions without metastasis were chosen and were matched as closely as possible. One group was biopsied, the other was treated without biopsy. Both groups received the same treatment, namely, the application of radium moulds Biopsies were taken with a sharp ring forceps and no subsequent coagulation was employed. The fact that the unbiopsied lesions may not all have been squamous cell cancers should favor contradiction of the results. The patients were followed at first monthly, then later at longer intervals. The follow-up time interval varied between $\frac{1}{2}$ and $\frac{4}{2}$ years. The lesions of 99 patients were biopsied and those of 67 were not The results are as follows

	 	-	
	Subsequent Regional Nodes	Distant Metastasis	l'otal
Biopsy (99) No biopsy (67)	16 (15%) 13 (19%)	3 (2%) 1 (15%)	19 (19%) 14 (20.5%)

Biopsy and Metastasis — There is good evidence from animal experiments that biopsy of a cancer does not increase

This controlled clinical experiment demonstrates quite clearly that the incidence of metastasis from squamous cell CANCER 855

carcinoma of the lip and mouth is no greater following biopsy than without it.

Radiation and Cancer-It has been noted by S. Warren et al17 that certain of the cervical carcinomas react poorly to radiation and progress steadily to a fatal termination. In an effort to select these cases for the purpose of applying additional methods of treatment, a group of 70 cervical carcinomas has been studied with respect to radiation effect as judged by postradiation biopsies. In some cases the biopsies were taken after the preliminary x-ray treatment, and in others after x-ray and radium application. Marked radiation effect was judged by the reaction of the tumor cells (diminished mitoses, necrosis, vacuolization of cell cytoplasm, disappearance of tumor cells) and by the reaction of the stroma (thickening, hyalinization, or necrosis of the vessel walls with thrombosis, increased stromal fibrosis, and marked hyalinization of the collagen). A moderate radiation effect was judged by the presence of the above changes to a lesser degree. In the group studied after preliminary x-rays, 90 per cent of the patients without biopsy evidence of radiation reaction died whereas 64 per cent of those showing a moderate reaction and 58 per cent of those showing a marked reaction died. In the group biopsied after x-ray and radium treatment, all patients showing no radiation reaction died whereas 70 per cent of those with moderate and 60 per cent of those with marked reaction died. The authors suggest that masmuch as those patients whose cervical cancers fail to show any radiation effect are very apt to die ultimately from cancer, they should be treated with surgery. Such a determination is most accurately reached by biopsy of the growth before radiation, after prelimmary x-rays, after radium, and 3 months following the last radiation treatment.

Subungual Melanomas—Subungual melanomas (nailbed melanomas of fingers or toes) were first described by Hutchinson in 1886. While this group forms only about 3 per cent of melanomas in general, the lesions are sufficiently numerous to constitute frequently a latent focus for generalized metastatic melanomatosis. G. T. Pack and F. E. Adair¹⁸ in a review of 85 cases point out that the most valuable sign of differentiation between this and other subungual lesions is a black halo in the skin about the involved nailbed. As the lesion progresses, it ulcerates the nail and exudes a dark, thin fluid. Benign nevi do not produce this ulceration. The differential list of subungual lesions with which melanoma may be confused includes paronychia, pyogenic granuloma, onychomycosis nigrescens (fungus), subungual hematoma, primary syphilitic chancer of finger, gangrene of the toe, subungual osteochondromas, subungual fibroma, subungual keratosis, subungual epithelioma, subungual angiosarcoma, subungual glomus tumors, and metastatic tumors of the nailbed. The treatment of subungual melanoma is immediate amputation of the digit. Routine dissection of the regional lymph nodes should be performed 2 weeks later in order to allow tumor cells in the lymphatics to reach the glands

The intermediate lobe of the pituitary secretes a hormone concerned with the function of pigment manufacture in the body P E Wigby and M. H. Metz¹⁹ conceived the idea that a connection might exist between this hormone and the abnormal growth of melanin-bearing cells. With this in mind the pituitary of a patient with widespread cutaneous and visceral metastases from a malignant melanoma of the face was subjected to intensive high voltage x-rays. He received a total of 1560 r. He improved almost immediately after the first treat-

ment. Most of the subcutaneous nodules disappeared and a nodule in the lung was reduced to half size as checked by x-rays Biopsy of a subcutaneous nodule before treatment showed markedly anaplastic melanomatous growth, whereas after pituitary radiation biopsy of a similar nodule displayed only granulation tissue and melanin phagocytosis. The patient had received previous to pituitary radiation splenic extract and radiation of the lung nodule without apparent effect. Following his x-ray treatment, he improved to such an extent that he was discharged from the hospital. The authors, encouraged with this striking result, employed similar deep roentgen therapy to the pituitary in 4 additional cases of widely metastatic malignant melanoma Practically no regression of the lesions resulted. These cases differed from the first in that all had lymph node involvement and none received splenic extract.

Lymph Node Metastases from Cervical Carcinoma—F J. Taussig²⁰ has pointed out that a certain number of lymph node metastases occur in cervical carcinomas of slight to moderate local extension. He cites the League of Nations classification in which cases with Group I local involvement have 15 to 25 per cent lymph node metastasis, Group II, 30 to 40 per cent, Group III, 50 per cent, and Group IV, 60 per cent. Since the chief objection to extensive pelvic dissection combined with complete hysterectomy is high primary operative mortality, the author proposes to destroy the growth locally by radiation and to remove the regional lymph nodes by laparotomy. These procedures the author found applicable only to cancers of moderate local extension (Groups I and II) From 1930 to 1939 the author performed 66 iliac lymphadenectomies for this type of cervical cancer The technic in general was as follows. (1) 4000 to 5000 r. deep x-rays over a period of 3 weeks, (2) 2 to 3 weeks after the above is concluded, a bilateral lymphadenectomy, (3) 2 to 3 weeks after laparotomy, 4500 mg.-hr. of radium applied to the cervix and uterine cavity Two deaths followed the laparotomies An average of 5 glands was removed in each case. Of 10 cases treated over 5 years ago, 5 are still alive (50 per cent), whereas in a control group of 35 cases only 7 have survived the 5-year period (20 per cent)

Radiation versus Resection of Infiltrating Carcinoma of Bladder-E Beer²¹ has made an interesting comparison between the end results of radiation and surgical resection of infiltrating carcinoma of the bladder. He points out that it is always difficult to implant radon seeds accurately into infiltrating vesicle growths. His statistics show that partial resection of the bladder for infiltrating carcinoma yields a 5-year cure rate of 18.5 per cent, whereas only 88 per cent of the cases receiving radon implants have survived 5 years. It is possible, of course, that the extent of the disease is not analogous in the 2 series reference to the curative value of deep therapy on moperable bladder cancers, Dr. Beer cites Lacasagnes publications from the Curic Institute to the effect that no bladder cancers beyond the resection stage have been cured with deep roentgen therapy. In 11 patients in which complete resection of the bladder for malignant tumors was possible up to 5 years ago, 5 have survived to the present This suggests that complete resection of the bladder gives the best long-term end results for operable infiltrating carcinoma

Roentgen Sterilization in Breast Cancer—The place of roentgen sterilization in breast cancer is still in some doubt. Certain cases of recurrent or inoperable carcinoma of the breast are un-

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doubtedly benefited. G W. Taylor²² reviewed 50 such cases and found that about one-third of them displayed temporary regression of the growth or definite clinical improvement following artificial menopause. The patients most benefited were those with osseous metastases. The author reviewed in addition a series of 47 women with operable breast cancer in which roentgen sterilization was done as a prophylaxis against recurrence. Fourteen of these had no axillary metastases and 33 had resectable nodes. No greater proportion of this entire group survived a 30-month postoperative period than did an analogous group without artificial menopause. Studies on the level of hormone excretion in the first groups indicate that the level of estrin excretion in the urine markedly diminishes after the production of artificial menopause.

Treatment with Cold — In 1938, Fay and G. C Henny²³ first published the data on the retrogression of tumor growth under the influence of cold. This investigation came about indirectly during neurologic experimentation on the determination of segmental skin temperatures by accurate thermocouple measurement It was learned that the average normal body surface temperature was 63° F $(35^{\circ}$ C) below the temperature of the mouth, and that on the distal portions of the extremities the temperature fell at times from 12° to 20° F (65° to 1110° C) below the buccal temperature It occurred to the senior author that such low peripheral temperatures might have a possible causal relationship with the infrequency of metastases to the extremities. Review of the literature substantiated the infrequency of extremity metastases but failed to elicit any reference to the effects of low body temperature on malignant cell growth

The authors designed a brine circulation apparatus which would depress skin temperatures by local application to from 45° to 60° F. (7.2° to 15.6° C.). Applications were made upon 5 patients with inoperable cancers of the breast or cervix or hypernephroma metastases. Definite local relief and partial regression of the tumor resulted In order to produce general lowering of body temperature, metabolic measures such as irradiation of the pituitary, thyroid and ovaries were tried. Later L. W. Smith and T. Fay24 much more effectively accomplished depression of general body temperature to 85° to 90° F. (29 5° to 32 2° C.) by withholding food, exposure of the body to temperature of 50° to 60° F (10° to 15.6° C) by air-conditioning if possible, light narcosis, and application of ice bags to the head and other parts of the body

This reduction of the body temperature (mouth) to below the critical level of 95° F. (35° C) is called hibernation in contrast to the local reduction of body temperature known as refrigeration. The authors have determined that the critical level of 95° F. (35° C) is apparently essential for the growth of undifferentiated tumor cells. On the other hand they have been able to reduce the temperature of parts of the body to 40° F. (4.5° C) for prolonged periods, and while control biopsies taken before and after treatment showed marked retrogressive changes in the malignant tumor as early as 24 hours after cold applications, the local normal tissue showed no indication of damage. Later tumor biopsies displayed actual tumor cell necrosis In order to reach distant metastases hibernation was used in conjunction with local refrigeration Rectal temperatures of from 85° to 90° F (29 5° to 32 2° C) were maintained from 1 to 5 days in 38 patients Marked clinical improvement

and no fatalities were listed following this treatment. This type of treatment is offered as a valuable adjunct to the methods already employed in the treatment of cancer.

Surgery of Primary Malignant Tumors—A good index of the success of surgical treatment for primary malignant tumors of long bones is available from a recent publication by C. C. Simmons ²⁵ He has reviewed the late results of treatment in 47 patients over 12 years of age Four of the 37 patients with osteogenic sarcoma refused treatment and were excluded from the series. Two of them were radiated for inoperable lesions, and 3 died within the 5-year period of other causes Of the remaining 28 cases of osteogenic sarcoma receiving surgical treatment, 39 per cent were 5-year cures Surgical treatment usually involved removal of the bone affected. These tumors lent themselves to segregation into 3 histologic groups: (1) Those composed mostly of fibrous tissue; (2) those composed of cartilage, and (3) those composed of anaplastic cells forming little cartilage or mature fibrous tissue. All of the 5 cases classified as the fibrous type of osteogenic sarcoma were alive in 5 years, 5 of the 7 cases of the chondral type, but only 1 of the 16 cases of the anaplastic type of osteogenic sarcoma survived the 5-year period All of the 8 patients with Ewing's sarcoma failed to survive 5 vears. One of 2 cases of reticulum cell sarcoma died of recurrence 12 years after the tumor's apparent removal, and another is alive 14 years after amputation, a recurrence having been removed from the operative stump 7 years after amputation The author does not employ preoperative radiation because of the delay. His procedure is to do a frozen section with a tourniquet on the limb and to amputate immediately if the diagnosis is sarcoma. In individuals over 50, the

osteogenic sarcoma frequently follows Paget's disease. The most interesting case in the series is a patient with the fibrous type of osteogenic sarcoma on whom a lobectomy was performed for 2 metastases of the lung 7 years after amputation of the humerus.

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ENDOSCOPY

By Louis H. Clerf, M.D.

BRONCHOLOGY

Hemoptysis

Difficulty often is experienced in determining the source of bleeding from the air passages particularly when repeated physical examinations and roentgen studies of the chest are negative. Gerlings and Polak¹ reported 2 cases of telangiectasis of the tracheobronchial tree. The first patient, a woman, aged 26 years, had frequent attacks of hemoptysis. Repeated studies proved negative for tuberculosis. At bronchoscopy, small varices were found in the trachea; in addition, areas of telangiectasis were observed on the soft palate, lips and about the face The second patient, a man, aged 41 years, spat blood often, had frequent epistaxis and on several occasions had severe hemoptysis Tuberculosis was suspected although the lungs were negative. The patient's father had a similar history and had many small varicosities over his lips Bronchoscopy revealed a small bleeding angioma in the trachea near the bifurcation and another in the lower lobe bronchus of the right lung. Cauterization of the varices with chromic acid applied bronchoscopically stopped the bleeding permanently.

Allergy

Chang² reported 2 cases of acute laryngeal obstruction that were proven to be definitely allergic in origin with specific sensitivity to milk. The larynx and gastrointestinal tract were involved in 1 while in the second case the tracheobronchial tree and larynx exhibited allergic manifestations. There was edema of the mucosa of the trachea and bronchi with much mucous exudation. In both

it became necessary to perform tracheotomy for relief of obstructive dyspnea.

Local treatment consisted of an ice coil about the neck, local application or hypodermic injection of epinephrine, cathartics to flush out toxins from the intestinal tract and tracheotomy for relief of dyspnea. Specific treatment should be directed at determining and eliminating the offending allergens. These cases emphasize the importance of considering allergy as an etiological factor in the management of cases of laryngeal obstruction.

In the experience of Friedman and Molony³ obstructive atelectasis in allergic patients may result from spasm of the bronchial musculature, thickening of the bronchial or bronchiolar walls, edema, hyperplasia, hypertrophy and cellular infiltration, the presence of thick tenacious mucus and paradoxic collapse of the larger bronchi during expiration

Treatment should be concerned first with giving relief to the patient and second, with the prevention of recurrence If the atelectasis persists in spite of ordinary methods as postural drainage and the employment of expectorants and epinephrine hydrochloride, bronchoscopic aspiration is the method of choice Repeated aspirations may be necessary before adequate ventilation of the air passages is secured.

Bronchoscopy in Unresolved Pneumonia

The term "unresolved pneumonia" often is loosely employed and frequently includes changes which have persisted for a considerable time following a pulmonary infection which was erroneously diagnosed as pneumonia.

McGibbon and others⁴ examined bronchoscopically 38 patients diagnosed incorrectly as suffering from unresolved pneumonia. Eight of these were found to be cases of bronchial carcinoma, 1 was suffering from an extrabronchial tumor of unknown origin, 2 from impacted nonopaque bronchial foreign bodies, 5 had bronchiectasis, 4 had pulmonary abscess, 1 had an inflammatory stenosis of a bronchus and in 1 there was bronchial compression from enlarged bronchial lymph nodes. In 18 children who exhibited varying degrees of incomplete bronchial obstruction secretion was found.

The cases which are diagnosed as unresolved pneumonia commonly are those in which there is partial bronchial obstruction with secondary bronchopulmonary changes distal to it. In cases of complete obstruction with pulmonary atelectasis the findings would differ greatly from those observed in unresolved pneumonia. The age of patients is important in this group. In children and young adults, bronchial obstruction is more often due to foreign body, secretions or enlarged lymph node. In adults, bronchial carcinoma is a common cause of obstruction.

Acute Laryngotracheobronchitis

Acutelaryngotracheobronchitis remains one of the most serious respiratory infections that has to be dealt with in children Richards⁵ has shown that in spite of the best-known methods of treatment the mortality rate is greater than 50 per cent. In a recent report on 17 patients with fulminating tracheobronchitis there occurred 7 deaths. Tracheotomy still remains the ideal method for relief of laryngeal obstruction. Although intubation has been advised the problem of obstruction to the lower airways cannot be met as readily in the intubated as in the tracheotomized patient.

Crusting of secretions in the trachea and larger bronchi may be relieved by repeated bronchoscopic removals Any measures that will counteract dryness of the inspired air and formation of obstructing masses of secretion must be employed. Among the many solvents employed, Richards has found nothing so effective as a solution of sodium perborate, frequently instilled into the trachea through the tracheotomic cannula and removed soon after by catheter suction. Since the Streptococcus hemolyticus is so frequently found in these cases sulfanilamide probably will be tried with increasing frequency. It was employed in 3 cases with but 1 recovery Further trial is needed to establish its value in this infection.

In the treatment of patients with acute laryngotracheobronchitis, Evans⁶ emphasized the importance of competent nursing care, maintenance of an adequate airway by tracheotomy, frequent aspiration of secretion through the cannula with bronchoscopic removal of crusts when indicated and humidification of the air. In 3 cases which recovered, 2 were due to a Staphylococcus albus and 1 to a Streptococcus hemolyticus. In the cases resulting from staphylococcus infection bacteriophage was instilled into the trachea through the cannula at frequent intervals and soon removed by suction Each instillation produced a paroxysm of coughing with evacuation of large quantities of viscid purulent secretion

In the experience of Font and Ortiz⁷ who reported 6 cases of acute laryngo-tracheobronchitis with 3 fatalities, the *Staphylococcus aureus hemolyticus* was found in all cases. The clinical course in their cases was not unlike that noted in cases due to the *Streptococcus hemolyticus*. The indications for treatment are

maintenance of an adequate airway and avoidance of dehydration.

In a series of 10 cases of acute laryngotracheobronchitis, Galloway⁸ reported 2 fatalities. He expressed the opinion that death resulted from cardiac and general exhaustion following occlusion of the bronchi by thick viscid secretion and edematous and inflammatory mucosa. In addition to tracheotomy and bronchial aspiration he recommended postural drainage employed in conjunction with instillation into the tracheobronchial tree of warm sodium bicarbonate or ephedrine solution and catheter aspiration through the tracheal cannula.

Neoplasm of Trachea and Bronchi

In a study of carcinoma of the trachea, Olsen⁹ added 9 cases that had not been previously reported. The symptoms, namely dyspnea, cough and stridor, are caused chiefly by certain mechanical factors and commonly are observed late. While these and the findings by roentgen study are important, tracheotomy and biopsy are essential for diagnosis in practically every case

The prognosis is unfavorable. Treatment is difficult and unsatisfactory due to late diagnosis and inaccessibility of the lesion. Surgical resection, local removal and cauterization with surgical diathermy through a bronchoscope or through the tracheotomy wound offer the best results

Two cases of carcinoma of the trachea, both occurring in women, were reported by Cann ¹⁰ The symptoms were unproductive cough, stridor and dyspnea. There were no voice disturbances; mirror laryngoscopy was negative. In both the diagnosis was made by biopsy, 1 by bronchoscopy and the other through the tracheotomy fistula

One of the cases was treated by **roent**gen therapy, the other by teleradium. In both, the tumor has disappeared and the tracheal obstruction has been relieved.

In the experience of Brock¹¹ the most frequently encountered benign bronchial tumor is the so-called adenomatous polyp. All benign tumors exhibit a marked tendency to bleed and to produce secondary pulmonary changes by causing obstruction followed by infection. Removal of the growth with forceps followed by the application of radium to the involved area is recommended.

The outlook for cure of carcinoma of the bronchus is unfavorable. Most satisfactory results are obtained by removal of the entire lung and adjacent lymph nodes. Unfortunately, the incidence of operability is not high. Next in order of preference is intrabronchial insertion of radon seeds rather than roentgen therapy. While complete cure is not anticipated by either the application of radon or roentgen therapy, the former produces local destruction of the growth, thus preventing complications incident to bronchial obstruction with suppuration.

Bronchial Foreign Bodies of Long Sojourn

In a detailed report of findings in 9 cases of bronchial foreign body of long sojourn, Butler and his co-workers¹² discussed the nature and significance of the pathologic changes consequent upon the prolonged presence of the foreign objects

Particular emphasis was placed upon acute suppurative pneumonitis and chronic suppurative bronchiectasis, 1 or both of which were observed in 7 of the 9 patients. It is reasonable to believe that they are evolutionary phases of the same entity and further, that chronic suppurative bronchiectasis, without or with bronchostenosis, is the probable fate of any patient who has survived prolonged obstruction of a bronchus by aspirated for-

eign body. When pulmonary suppuration has become established, neither removal of the foreign body nor other palliative form of treatment is adequate to affect a cure. *Extirpation of the damaged lobe* or *lung* is indicated.

Pneumonography in Pulmonary Abscess

An absence of clinical symptoms referable to a suppurative process and the dis-

be employed routinely in these cases to ascertain the condition of the bronchial tree and that the clinical concept of healing of pulmonary abscess should include the residual changes in the bronchi and lungs.

Bronchoscopy in Bronchiectasis

In discussing the development of bronchiectasis, Holinger¹⁴ emphasized the importance of recognizing those forms





Fig 1—Radiograph showing early triangular shadows at the right base which persisted 2 months following an "atypical pneumonia". The child had cough and low-grade fever, with physical findings of dullness and bronchial breathing at the right base. (Holinger: Ann. Otol. Rhinol. and Laryng.)

appearance of the roentgen shadows of pulmonary abscess and surrounding pneumonitis commonly are accepted as conclusive evidence that an abscess of the lung has healed In a study of a group of cases of apparently healed pulmonary abscess, Franklin¹³ found that residual pathologic changes in the lung and bronchi often may be demonstrated by instilling iodized oil for lung mapping He concluded that this procedure should

of bronchial inflammation which, producing bronchial obstruction and atelectasis, eventuate in bronchiectasis unless prompt relief is afforded. The physical findings and roentgen shadows of a triangular basal lesion often suggest a diagnosis of pneumonia. The clinical course, however, is atypical. Physical signs commonly persist and there are clinical evidences of lower lobe atelectasis. The roentgen findings confirm this and show

a triangular shadow at the base of 1 lung (Fig. 1).

The bronchoscopic findings in such cases are of utmost importance. The bronchus of the involved lobe is found inflamed and contains a moderate quantity of viscid pus Removal of this reveals an inflamed and edematous stenotic lumen with thick pus oozing from the orifices of the swollen bronchial sub-

that in cases of long standing repeated bronchoscopic aspirations and bronchial dilatation were necessary to reestablish normal function.

In cases of several years' duration, restoration of function may be impossible although bronchoscopic aspiration will aid materially in reducing the quantity of sputum and change its foul character.





Fig. 2—Radiograph of same patient as shown in Fig. 1 made following bronchoscopy. Dilatation of the inflammatory bronchial stenosis and aspiration of the obstructing purulent secretion, which produced the atelectasis, resulted in prompt reaeration of the involved portion of the right lower lobe (Holinger Ann Otol Rhinol and Laryng)

divisions () ften no air bubbles are observed in the pus indicating that air neither enters nor leaves that portion of lung which is atelectatic. In a large number of cases there was prompt clearing up of the involved area following the initial bronchoscopy (Fig. 2). These cases can still be considered as definitely "prebronchiectatic." Every effort should be made to clear them up as promptly as possible for it has often been noted

Bronchoscopy in Tuberculosis

During the past few years bronchoscopy has gained prominence as an aid in diagnosis and treatment of pulmonary tuberculosis. The information gained by this procedure has been most helpful Despite this there will arise a question whether bronchoscopy had any deleterous effects on the patients examined.

Advocating routine bronchoscopic examinations in all cases of active pulmo-

nary tuberculosis, McIndoe and others¹⁵ examined 272 patients over a period of more than 11/2 years There was an increase in the pulmonary disease in only 4 patients on the basis of a comparison of the pre-and post-bronchoscopic roentgenograms In some cases the quantity of sputum was increased for a few days following bronchoscopy but there were no significant changes on the basis of the number of tubercle bacıllı found There were temperature rises in a small group of patients but these were not regarded as significant There was no apparent lasting increase in the laryngeal reactions

The information gained by bronchoscopy was noteworthy. Eleven per cent of the patients showed evidences of tuberculous involvement of the trachea or bronchi based on the appearance of the lesion rather than histological examination. Persistant oral wheeze was the symptom most frequently encountered Bronchial obstruction, unexplained spread of the tuberculous infiltration or atelectasis were most commonly encountered with tuberculous tracheobronchitis.

In a bronchoscopic study of 516 tuberculous patients, Hawkins¹⁶ found gross evidences of tuberculous bronchits in 132. In a majority the involvement was unilateral. There was extensive ulceration of a major bronchus in 43 with extension into the trachea in 27 instances. In several a main bronchus was completely occluded.

Although bronchoscopy in tuberculosis has not been routinely employed by the author it has been performed on patients who exhibited certain of the classical symptoms and signs of tuberculous tracheobronchitis, namely asthmatic attacks, wheeze, rhonci, dyspnea out of proportion to vital capacity, excessive cough with tenacious sputum, constant tendency to clearing of the throat and

persistently positive sputum with no other evidences of pulmonary tuberculosis.

The discovery by Benedict¹⁷ of bronchial stenosis by bronchoscopy in 3 patients in whom thoracoplasty had been performed for pulmonary tuberculosis indicated the need for preoperative bronchoscopic study. The stenosis presumably was caused by a preexisting tuberculous tracheobronchitis. Gradual dilatation of the stenosis and aspiration of secretions were carried out with marked benefit to the patients Repeated dilatation is recommended to prevent recurring stenosis.

Bronchopulmonary Aspergillosis

The paucity of reported cases would indicate that invasion of the lungs by aspergilli is uncommon In the patient with bronchopulmonary aspergillosis reported by Stolow¹⁸ a diagnosis of pulmonary tuberculosis had been made although no tubercle bacilli were found There was a history of cough which developed while he was threshing oats. The bronchoscopic findings were not siginficant, secretion removed for bacteriological study revealed an aspergillus. The importance of the history and studies of sputum for fungi in patients suspected as tuberculous but with negative sputum is recommended

ESOPHAGOLOGY

Cicatricial Stenosis

In an analysis of 50 cases of stricture of the esophagus, Martin and Arena¹⁹ found 48 due to the ingestion of lye. The common site of stenosis was the upper third of the esophagus. In 10 the strictures were multiple. Following the initial symptoms there was usually a brief period of no apparent dysphagia.

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They advocated the passage of a mercury-filled catheter beginning 4 days after the accident if edema and inflammation have subsided sufficiently. Peroral bouginage, employing a string as a guide, retrograde bouginage through a gastrostomy opening, peroral esophagoscopic or retrograde gastroscopic bouginage must be used in treatment if cicatricial stenosis has developed.

The ease of perforation of the esophagus must constantly be borne in mind by anyone undertaking the treatment of any type of esophageal stricture. Heatly²⁰ emphasized the importance of varying the method of treatment with the experience of the physician himself. It is imperative that the general condition of the patient receive primary consideration before local measures are attempted. All blind methods of treatment as well as over-rapid or excessive dilatation should be avoided. Dilatation should be carried out under visual guidance or by employing a previously swallowed string as a guide. It is important to keep the patient under observation for months after the conclusion of active treatment if successful results are to be secured

Periesophageal Abscess

The most frequent site of perforation of the esophagus is at the level of the cricopharyngeus. In a study of periesophageal abscess, Hunt²¹ found that the causes were injury due to foreign body, instrumentation and spontaneous rupture accompanying malignancy an analysis of 20 cases of periesophageal abscess he found that in 17 the perforation was produced by foreign body, in 2 it followed biopsy and in 1 it occurred following instrumentation. The roentgen study often is the determining factor in diagnosis and aids in differentiating between simple cellulitis and abscess formation with a bubble of air.

Sixteen of the 20 cases were operated on by external drainage with 12 recoveries and 4 deaths. Four cases, all of which terminated fatally, were not operated on but were treated either conservatively or esophagoscopically. Hunt expressed the opinion that external drainage gives the best results. Any rise in the temperature and leukocyte count, pain and particularly roentgen evidence of periesophageal involvement necessitates immediate external incision and drainage Intraesophageal treatment should be employed only in selected cases.

Peptic Ulcer of Esophagus

Two conditions necessary for the production of peptic ulcer of the esophagus are the presence of gastric mucosa in the lower portion of the esophagus and a patent cardia through which gastric juice may be regurgitated. Chamberlin²² suggested that the patency of the cardia might be caused by congenitally short esophagus or hiatal hernia. In 7 cases reported by him one or both of these conditions were present Among the criteria necessary for the diagnosis of peptic ulcer of the esophagus is visualization of the ulcer by direct examination.

Foreign Bodies

In an experience of 200 esophagoscopic examinations in patients suspected of having a foreign body lodged in the esophagus Wrigley²³ found and removed a foreign body in 180. In 6, the foreign body was seen but passed into the stomach, in 1 case it was seen but was immovable and in 13 the examination proved negative. In a number of cases where there was a history of swallowing some object and the roentgen report indicated the presence of a residual flake of barium, the esophagoscopic examination was negative; however, a foreign body was found sufficiently often to jus-

tify routine esophagoscopy. Wrigley emphasized the importance of diagnostic esophagoscopy in all cases in which the roentgenologist is unable to give an absolutely negative report.

GASTROSCOPY

Gastroscopy for Diagnosis

Although the value of flexible tube gastroscopy in early diagnosis of gastric carcinoma may be disputed, gastroscopists recognize its value in differentiating between benign and malignant lesions in determining operability of the latter. Schindler and Gold²⁴ expressed the opinion that gastroscopy facilitates early diagnosis of gastric cancer and often is superior to all other diagnostic methods They emphasized the importance of considering gastroscopy as being supplementary to and not competitive with roentgen study. Cases are cited in which gastroscopy aided in diagnosis of cancer in the absence of other data, in corroborating the roentgen diagnosis and in determining operability

In a gastroscopic study of 143 patients to determine the incidence of chronic gastritis, McNeer and Barowsky²⁵ found that in over 50 per cent some form of gastritis was found pres-In their experience the clinical, laboratory and roentgen studies give little information in a majority of these cases, the exception being advanced hypertrophic gastritis where roentgen study may make such a diagnosis. Pathological corroboration of a diagnosis of gastritis is difficult because of rapid postmortem autolysis of gastric mucosa.

In a report on the gastroscopic findings in 23 patients with pernicious anemia, Schindler and Serby²⁶ found no evidence of appreciable improvement in the appearances of the gastric mucosa in 4 of 14 that received treatment. In the remaining 10 treated patients almost complete regeneration of the mucosa occurred In 9 that did not receive treatment there were evidences of atrophic or superficial gastritis, either diffuse or patchy, distributed both in the antrum and body of the stomach.

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GYNECOLOGY

By P. Brooke Bland, M.D., and Arthur First, M.D.

AMENORRHEA AND STERILITY

X-ray Therapy — I. I. Kaplan¹ reestablished menstruation in 124 of 142 amenorrheic women. All of the women received roentgen therapy to the pelvis; 104 were given additional therapy to the pituitary and in 6 the thyroid also was treated. The amenorrhea in these women has persisted for from 1 month to 14 years and sterility from 1 to 18 years. The oldest patient was 45 and the youngest 19 years of age. The data show that the younger the patient, the more successful the results Those most successfully treated were within the 21 to 29 year group There were 52 subsequent instances of pregnancy Of the 52 who conceived, 17 did so more than once Five women aborted; 2 of these aborted twice

Forty-four went to term and delivered 50 normal babies, 1 woman was pregnant; in 1 woman an ectopic pregnancy developed which was terminated by operation, and 1 bore an abnormal child In the group of living children there were 27 boys and 23 girls, and reports from their parents have disclosed no abnormalities or physical deformities Because of the success achieved with irradiation, the author reiterates his previous conclusion that irradiation, when properly employed, is not harmful to the mother or to the offspring and that it has proved a valuable therapeutic procedure for the treatment of amenorrhea and the relief of sterility

BLADDER, URINARY

Postoperative Care — J. D Wood-ruff and R W. Te Linde² advocate instilling into the bladder 1 ounce (30 cc)

of 0.5 per cent aqueous solution of *mercurochrome* in the operating room. The results after pelvic laparotomies have been very gratifying, the incidence of catheterization having been reduced from 51 per cent in a control series to 65 per cent in a series of 500 cases in which this procedure was used. An instillation of a liter of fluid by rectum at the same time was found to be of no value in reducing the incidence of catheterization.

Evidence is presented to show that the patients in whom the instillation was used voided earlier and in greater amounts, thus more completely emptying the bladder than the patients in the control series. The shorter the anesthesia the greater the likelihood of spontaneous postoperative micturition. The patients receiving a basal anesthesia of averting with amylene hydrate required catheterization in 8.2 per cent while those given straight gas, oxygen and ether required catheterization in only 3.7 per cent.

Postoperative urmary tract infection, as judged by symptoms of cystitis on discharge and pyelitis, did not occur after any of the 500 laparotomies in which the procedure was carried out, with the exception of 3 cases. In each of these there was a definite history of urmary tract infection preoperatively. The procedure has been shown to be of no value in case of extensive plastic operation, in which an indwelling male catheter is considered the most satisfactory procedure.

CERVIX UTERI

Carcinoma

Diagnosis—H Wespi and D Brasch³ report the clinical observations in 9 cases of primary carcinoma of the cervix.

These observations extended over more than 2 years, the authors employing the colposcope, the iodine test and microscopic analyses on the basis of Hinselmann's classification. The age of the patients ranged between 32 and 52 years, with an average of 41 5. The authors' purpose was to arrive at a comparative evaluation of the microscopic and colposcopic pictures and a rapid survey of the extension and nature of histologic modifications. Serial sections were performed on 8 patients.

The 9 patients were divided into 3 groups. In group 1 (5 patients) carcinoma was discovered only through the colposcope In group 2 (2 patients), colposcopy confirmed macroscopic suspicions. In group 3 (2 patients), 1 case of carcinoma was detected without the colposcope, in the other case, the malady was too deep seated to admit of colposcopic determination. In their epicritical comments, the authors point out several microscopic peculiarities. Besides areas with manifest inward penetration and pronounced atypias of a caremomatous nature there were extensive portions with marked atypical epithelium but without any indications of penetrating growth, an indication of cancer of multicellular origin, the connection established by an atypical epithelium, called "matrix" by Hinselmann In 3 patients, abnormal epithelium was found besides the atypical

Nearly all of the 7 patients successfully examined with the colposcope revealed various modifications, such as leukoplakia, to which, according to the authors, no undue significance should be attached. Coarse, heavy proliferations and red surfaces that bled easily on being touched along with other "matrix" areas invited suspicion of the presence of a carcinoma. Whenever the atypical epithelium extended beyond the colposcopically suspected areas, application of the iodine test

adjudicated the doubt. The authors state that they employed the Schiller test with greater frequency to distinguish patients with atypical and hence carcinomatous epithelium from those with abnormal epithelium. None of their patients showed the characteristic symptoms of early carcinoma, such as bleeding on contact and bloody discharges. They therefore stress the significance of the period of latency and emphasize the value of precautionary examinations, if the colposcope and iodine tests are resorted to from the beginning.

Treatment — This paper by J. V Meigs and H. L. Jaffe⁴ presents 70 patients who have been followed and studied very carefully It shows that the results of the treatment of cancer of the cervix with x-rays and radium are eminently satisfactory It is evident that certain charts of prognostic value can be made and the curves induce the authors to beheve that it is no longer necessary to follow patients for 5 years before reporting on them but that a 3-year follow-up from the time of treatment should suffice If, from the end results at 3 years, 15 per cent is deducted for the next 2 years, the approximate 5-year results can be predicted. Therefore, more opportunities are given to the gynecologist and radiologist to change a given form of treatment

The authors believe that the routine study of microscopical slides, while the patient is being seen, is of great value. The presence or absence of a proper microscopical radiation reaction is an important prognostic sign. The authors advise that in every cancer clinic the slides be looked at at the same time that the patients are examined.

Biopsies should be taken before treatment starts and after treatment to determine whether or not radiation is satisfactory as determined by the radiation reaction.

In this series of cases it is evident that kidney lesions due to blocked ureters with subsequent uremia are among the chief causes of death. It is the feeling of the authors that more urological investigation should be undertaken and it should be undertaken before, during, and following treatment. Any indication of ureteral block should be treated early rather than late.

Chronic Cervicitis

Treatment—The treatment of chronic cervicitis is discussed by W. T. Black.⁵ Topical applications are advised by some physicians. Black has not found them particularly effective. A cervical infection confined to the portio vaginalis and associated with vaginitis should, of course, be treated along physiologic lines, *i. e.*, by keeping the vaginal flora at the normal pH of 4 or 4.2

The surgical treatment of chronic cervicitis consists of amputation, a Sturmdorf operation or a trachelorrhaphy. In the elderly, a badly diseased cervix, especially if elongated, lacerated or prolapsed, should be completely removed Amputation may also be performed in younger women who are sterile

When the cervix is elongated and hypertrophied, a modified Schroeder or Sturmdorf operation is advisable. In the presence of an extensive laceration, trachelorrhaphy is indicated. A laceration of 1.5 cm or less is best treated with the cautery. Electrosurgical operation is the method of choice for chronic cervicitis, as it gives excellent results and reduces the danger of cancer. Cauterization or conization is preferable to electrocoagulation in that they are less often followed by infection. Electrocoagulation, moreover, interferes with the obtaining of a complete biopsy specimen.

For a superficial endocervical lesion, lineal applications of the smallest cautery point are sufficient for mild cervicitis and the cautery should be lightly applied; deep cauterization or conization should be avoided. For a small cervix with a persistent mucopurulent discharge, repeated light cauterization is preferable. For more advanced infections, deeper lineal burns are necessary. For the hypertrophied cystic cervix, conization, followed by destruction of cysts left by the cautery point, is the proper treatment. A laceration, if present, may be cauterized at the same time Rarely is amputation required, even in the presence of extensive disease In any case, one should avoid entering the uterine cavity, as this adds materially to the danger of infection.

In the postoperative care, the patient should be warned that the leukorrheal discharge will increase and informed of the probability of bleeding within 10 to 14 days and the possibility that the following menstrual period will be prolonged. She should also be instructed to begin taking douches after 2 or 3 days unless the uterus is retroverted and the cervix patent; in this event, the douches should be postponed. Coitus should be discontinued for 1 month. The patient should see her physician within 10 days, again 2 weeks later and thereafter once each month for 4 months or longer.

At the patient's first visit, the physician should avoid loosening the exudate for fear of hemorrhage. A germicide is gently applied to the endocervix at subsequent visits; after 1 month, dilation of the cervix may be necessary. The mucous membrane regenerates, epithelizes and becomes normal in appearance and function except for a deficiency of mucous secretion.

Stenosis, atresia, cellulitis, pelvic abscess and even peritonitis with death are

possible sequelae of improper operative treatment or postoperative care.

Tuberculosis

Tuberculosis of the cervix uteri is discussed by D. C. Collins ⁶ Among 33,580 reported instances of female genital tuberculosis there were 133 (0 3961 per cent) of tuberculosis of the cervix uterine Of these 133 cases, 13 (9.776 per cent) were undoubtedly instances of primary tuberculosis. In approximately 42 per cent of these cases there was associated active pulmonary tuberculosis.

Tuberculosis of the cervix uteri is. in approximately 85 per cent of cases, secondary to a tuberculous focus elsewhere in the body Such primary foci may be found in the lungs or in either the gastrointestinal or the genitourmary tract. Of the 185 cases which the author studied from the literature, in 156 (84 per cent) there was demonstrable tuberculosis elsewhere. In 102 cases (55 131 per cent) genitourinary tuberculosis was present in either an active or a quiescent stage Marriage and pregnancy are 2 common contributing etiologic factors Tuberculosis of the female generative tract occurs most frequently in the fallopian tubes and progressively diminishes in frequency as it approaches the uterine It is believed that this disease usually results from a descending infection spread by contiguity from foci situated higher in the pelvis or by hematogenous and lymphogenous routes from distant foci

Primary tuberculosis of the uterine cervix is rare. In this series of 185 cases studied from the literature there were 16 proved instances of this type of primary infection.

Tuberculosis of the cervix uteri is classified into 4 types. The ulcerative; the papillary, the miliary, and the rare bacillary catarrhal Thus the gross appear-

ance of the cervical lesion may vary widely. The typical lesion is usually ulcerated

Secondary infections are commonly superimposed on these lesions. Varying degrees of bleeding or even severe hemorrhages with accompanying foul leukorrhea are frequently encountered Microscopically, typical tubercle formation is not commonly seen Often atypical tubercles composed of only epithelioid and lymphocytic cells may be the only evidence on which a presumptive diagnosis of tuberculosis can be made Acid-fast stains for the presence of the tubercle bacillus in either the microscopic section or the tissue smear may be apparently negative Inoculation of guinea pigs may prove to be the only reliable method by which a correct diagnosis can be established. Biopsy is a quick method of establishing a probable correct diagnosis

In 100 ulcerated lesions of the cervix which grossly resemble a neoplasm, the physician could correctly diagnose the lesion as being caused by a carcinoma in 98. The disease must be differentiated from lesions resulting from hypertrophy of the cervix accompanied by eversion and erosion, myomatous or polypoid changes, gonorrhea, syphilis, actinomycosis, sarcoma and principally carcinoma

Treatment- The treatment of tuberculosis of the uterine cervix should preferably be of a radical surgical character,
such as *abdominal panhysterectomy*with the possible preservation of 1 ovary,
if the patient's condition and other factors are favorable, because usually extensive tuberculous disease of the upper
pelvic part of the generative tract is present and must be eradicated if cure is to
result. For that reason and because of
the rarity of a primary tuberculous infection of the cervix, local treatment of the
cervical lesion is not advisable. For similar considerations, roentgen and radium

therapy will often prove disappointing in their end results. The contraindications to the employment of surgery are advanced local tuberculous lesions with extensive involvement of the neighboring bladder or rectum, extensive tuberculous salpingitis, marked secondary infection, the presence of active tuberculous foci elsewhere, cardiovascular disease and senility. The ultimate prognosis in this disease entity is dependent on the type of treatment employed and on whether active tuberculosis is present elsewhere in the body.

DYSMENORRHEA

Treatment-U. J. Salmon, S. H. Geist and R. I Walter⁷ report a group of 30 patients with dysmenorrhea who were treated with testosterone propionate. The level of testosterone tolerance was established at approximately 500 mg Administration of upwards of 500 mg. resulted in the appearance in some of the cases, of (a) masculinization phenomena, viz., hoarseness of the voice, facial hirsutes, slight enlargement of the clitoris; and (b) evidence of estrogen deficiency, vis, suppression of menstruation, atroplue vaginitis, varying degrees of hypoplasia of the endometrium, and "negative" vaginal smears.

The suggestion is made that the biologic effects of testoserone propionate (in doses of 500 mg, or more) in women is brought about by inhibition of the gonadotropic factors of the hypophysis with consequent suppression of ovulation, estrogen and progesterone formation and menstruation, as well as by inactivation of the circulating estrogens and estrogen stores in the body.

Normal cyclical phenomena (clinical and morphologic) returned spontaneously in all cases within 2 months after treatment. With doses of 300 mg or less,

neither androgenic nor estrogen deficiency effects were produced.

In the treatment of dysmenorrhea the dosage of testosterone propionate recommended is 250 to 300 mg. given during 1 cycle. Symptomatic relief was achieved in 26 of the 30 cases. The therapeutic effects noted with smaller doses of testosterone propionate are probably the result of partial mactivation or modification of the action of the estrogens and progesterone.

ECTOPIC PREGNANCY

A review of 310 operative cases of ectopic pregnancy is reported by L. Langman and M Goldblatt.⁸ In these cases there is an unusually high incidence of previous lower abdominal surgery

Although a history of pelvic infection was obtained in less than 20 per cent of our cases, microscopic examination of the tubes showed evidence of inflammation in more than 50 per cent. The authors find that overemphasis has been placed on the sterility period prior to the occurrence of an ectopic pregnancy. The number of previous pregnancies or their termination bears no relation to the incidence of ectopic pregnancy.

Pain is most often colicky, severe, irregular, and generalized over the abdomen. Radiation to 1 or both shoulders is relatively uncommon, but significant when present. Nausea and vomiting are far more frequent than fainting. The latter, when present, is pathognomonic. Pain and bleeding in relationship to the last menstrual period is extremely variable as to occurrence, duration, and amount, and often difficult to correlate

Physical findings without laboratory aid are often misleading. The sedimentation rate is most often normal in spite of an elevated white count. In doubtful

cases, the Aschheim-Zondek test (or Friedman modification) is indispensable. Excluding abortions and normal intrauterine pregnancies, a positive test always means ectopic pregnancy.

The use of repeated whole-blood transfusions before, during, and after the operation should reduce the mortality to less than 2 per cent. The percentage of error in this series was 29.7 The commonest cause of error was chronic salpingo-oophoritis. This, it is believed, can be greatly reduced by the more frequent use of the Aschheim-Zondek test.

More than two-thirds of the cases of ectopic pregnancies in this series occurred in the ampullary portion of the tube, as has been reported by other investigators. Pathological examination of the tubes removed revealed inflammatory reaction both acute and chronic in over 50 per cent of the cases.

ENDOMETRIOSIS

Treatment—The treatment of endometriosis is discussed by V. S. Counseller 9 Removal of both ovaries or their destruction by radium or roentgen ray would render all endometriomas inactive, but unfortunately most cases of endometriosis occur during the most active reproductive period of life, that is, in the third and fourth decades. However, too much emphasis should not be placed on this for the author has found that 489 per cent of 131 married patients with this disease either had never been pregnant or had had only miscarriages The absolute sterility was 32 1 per cent Furthermore, following conservative surgery in these patients in 55 cases in which pregnancy could have reasonably been expected, it actually did occur in only 7 patients, resulting in a total of 10 children.

Counseller feels that patients in the third and fourth decades of life at least should be submitted to surgical treatment rather than to radium or roentgen therapy, because it is impossible to determine clinically whether complete cessation of function of the ovary is advisable. Furthermore, it is much wiser to know whether there is any other associated pathologic condition of the pelvic organs before submitting the patient to castration by radium or roentgen rays The 1 exception to this rule may be a large adenomyoma of the rectovaginal septum which cannot be removed surgically without considerable risk of producing a rectal fistula

The relief of dysmenorrhea due to endometriomas is a simple matter when these are confined to the uterine musculature. Since the pain from the uterus is purely a visceral pain it should be adequately relieved by a presacral neurectomy together with complete excision of all uterine endometriomas.

At the Mayo Clinic the surgical treatment consists in preservation of 1 or both adnexa where possible, and complete excision of all adenomtaous tissue involving the uterus, in these patients a *presacral neurectomy* is routinely performed. Also, complete or partial excision of all heterotopic endometriomas is done with the surgical diathermy wire loop.

If the disease does not lend itself to these conservative procedures, then radical removal of all pelvic organs is performed regardless of the age of the patient

HEMORRHAGE

Newer Concepts in Control — Recently A. Steinberg and W. R Brown have been working on the problem of blood coagulation and have presented their findings in a paper read before the

American Physiological Society at its 1939 meeting.¹⁰ Extracts have been prepared from certain plants which have been found to accelerate the rate of the coagulation of the blood markedly and rapidly. The best plant sources have been found to be shepherds' purse, wood sorrel beets, oxalis, citrous fruits, alfalfa

Similar extracts were prepared from placenta, cord blood, spleen, liver, bile, etc., which also possessed marked hemostatic properties.

From these preparations, Steinberg and Brown isolated colorless monoclinic crystals, having a melting point of 212° F (100° C.) and which possessed most of the clotting power of the extract. These crystals were identified as oxalic acid. Solutions of pure commercial oxalic acid were prepared in the same concentration as present in the extract and were found to possess the same power to reduce coagulation time in the rabbit as the extracts themselves.

A titrametic test for oxalic acid in the blood was devised and normal values for human beings were established at 5.5 to 7.5 mg per 100 cc. Elevations in clotting time were attended by a fall in the blood oxalic acid, while reductions in clotting time resulted in a rise in the oxalic content of the blood. Cord blood was found to contain as much as 17 mg per 100 cc, while maternal blood immediately postpartum also showed a considerable elevation in the blood oxalic acid. In both instances, the clotting time was appreciably reduced.

The clinical application of the study in gynecology and obstetrics is described by E. A. Schumann.¹¹

The extract from certain plant substances containing as its principal active agent oxalic acid, possibly with the little understood vitamin K, has been put up for the market under the name of **koagamin**, a sterile solution for intravenous

and intramuscular administration. The oxalic acid content is 1 mg. per cc. and the usual dose is 3 cc. intravenously followed by 2 cc. intramuscularly at intervals of from 3 to 4 hours. The effect on coagulation time becomes apparent after 10 or 15 minutes and lasts for about 8 hours. Much larger amounts have been administered without any appreciable ill effects. The material is of value in hemorrhage of any type, but experience has shown that several modifications in administrative methods are necessary in certain types of bleeding.

In cases where hemorrhage is associated with increased permeability of the blood vessels as melena, the purpuric state, etc., the effect of koagamin is much enhanced if the patient be given massive doses of vitamin C for several days. Preceding the exhibition of the coagulant present, it is well to inject a donor with koagamin 15 minutes before a blood transfusion, under which circumstances the maximum effect is obtained

The use of this material has since become routine with the author in all cases of melena neonatorum. In post-partum hemorrhage and in placenta previa, its action has been satisfactory, although more difficult to evaluate since bleeding of this type often ceases spontaneously. In a number of cases the dissection is almost dry, unless a spurting artery is cut, whereas in the other the usual venous ooze will be seen.

Whenever koagamin is giving during or immediately after the course of an operation its use is continued for from 24 to 48 hours, after which much danger of hemorrhage has usually ceased. In uterine bleeding, either of the functional type or, more particularly, the bleeding from fibroid tumors of the uterus, koagamin exerts an active influence.

In fibromas the hemorrhage usually ceased within 20 minutes after the in-

travenous injection of the drug and, while it may recur, the quantity of blood loss has been definitely much less after the injection than before. Hemorrhage of functional origin yields also to this preparation in rather dramatic fashion, although the theoretically correct treatment of the hyperplastic endometrium with antuitrin-S should not be neglected After difficult pelvic enucleations, the oozing raw surfaces in the cul-de-sac which are not capable of being covered by peritoneum may be rendered quite bloodless by the use of koagamin

With regard to the danger of oxalic acid given intravenously and intramuscularly, Schumann states that this drug has been given to something over 1200 patients, often in repeated doses. Not only have no deleterious effects been observed, but they have not yet noted a single reaction of any sort. He therefore feels that the danger is negligible. It is to be remembered that oxalic acid taken by mouth is often fatal

MENOPAUSE

Ovarian Hypofunction Previous to Climacteric—L F Hawkinson¹² discusses the results of estrogen therapy in 300 cases of menstrual disorders associated with ovarian underfunction Patients with an artificial menopause and, when possible, those with the natural menopause were excluded. Also all patients whose symptoms might be accounted for by organic complications were eliminated. The patients' ages ranged from 14 to 35 years, with an average age of 27 years. The average duration of symptoms was 14 months with the exception of 34 patients who complained of symptoms since the menarche than one-third of the patients had symptoms soon after pregnancy or abortion

and more than 12 per cent after salpingectomy or the removal of 1 ovary

The symptoms, as in the menopausal syndrome, are due primarily to a deficiency of estrogen and, with the exception of the menstrual disturbances and the changes in the vaginal smears, are of a subjective nature Nervousness was an almost constant complaint but was seldom objective in type. Fatigability and lassitude were almost as prevalent as nervousness. Almost 40 per cent had disturbances of sleep Excitability and irritability, reflected by exaggerated response to slight emotional shocks, were common Gastric disturbances, cardiac symptoms and vague and indefinite pains occurred in many cases without demonstrable pathologic changes The commonest cardiac symptoms were palpitation and tachycardia. Flushes and chills were complained of by 18 per cent of the women Headaches were complained of by 46 per cent of the patients. Of the 265 who had definite menstrual disturbances, 174 suffered from scanty menstruation Eighty-nine had dysmenorrhea and an almost equal number had irregular menstruation Menorrhagia. metrorrhagia and secondary amenorrhea were not as common

Treatment \ number of patients had 2 or more disorders of menstruation Many patients stated that there was a difference in intensity of the symptoms month by month, suggesting the involvement of 1 ovary. Only standardized estrogenic preparations were used in treatment. The amount of estrogen required to relieve symptoms varied with each patient. Some patients responded to oral therapy alone, while others required as much as 10,000 International Units (2000 rat units) of estrogen in oil by hypodermic injection 3 times weekly Initially the oral preparations were usually administered If there was no response

within 3 to 4 weeks, larger doses of estrogen in oil were administered intramuscularly. Combined oral and hypodermic therapy was of advantage in the severe cases After a satisfactory response had been obtained, the dose was gradually reduced, and only when the patient remained free from symptoms was it discontinued The average patient required treatment for 3 or 4 months. However, 57 women required continuous oral treatment to remain symptom free. With the exception of an occasional local reaction at the site of injection, no ill effects were observed The subjective symptoms responded more favorably than did the associated menstrual disturbances.

Data show that 44.3 per cent were relieved of the majority of symptoms, 31 per cent were improved and 247 per cent experienced little or no relief. Fortyfour patients (74 5 per cent) found that estrogen decreased the severity and frequency of attacks of menstrual migraine Fourteen (318 per cent) obtained complete relief from headaches Of the 78 women who complained of occipitocervical aching, 61 were relieved. Of the 54 patients who had a low hemoglobin with or without a corresponding decrease in the number of erythrocytes, 29 (574 per cent) showed improvement in the hemoglobin level and number of erythrocytes following the administration of estrogen

By the administration of from 30 to 50 mg of testosterone propionate L Kurzrok, C. H Birnberg and S Livingston¹³ were able to ameliorate almost completely the symptoms of the menopause in 21 cases. The substance produced no effect on the breasts, in that no patient complained of mastalgia One patient with arthritis accompanying the menopause was benefited. There were no instances of itching or discharge due

to the male sex hormone. Several of the younger women who had had a surgical menopause with resulting markedly severe symptoms responded fully as well as those in whom the menopause was spontaneous. One patient, with severe diabetes, was relieved of her flushes and sweats without any effect on the status of the diabetes A few patients complained of localized pruritus on 1 occasion only, at the site of injection. Three patients had been treated previously with large doses of estradiol benzoate after a radiation menopause, with subsequent uterine bleeding; none of these women had any bleeding following administration of the male hormone.

MENSTRUATION

Causation—Earl T. Engle¹⁴ offers a brief recapitulation of the stages which permit our present interpretation of the rôle of the sex hormones The first experimental observations were those of Allen, which were the basis for the estrin withdrawal theory which he and many other observers still maintain. There is no doubt that withdrawal or reduction of the estrogen level by any means results in typical uterine bleeding. The high incidence of anovulatory menstrual cycles in the monkey, especially those in captivity, makes this animal an excellent form for those who would elaborate and justify this theory

It is, however, obvious that, interesting as the observations may be, they do not explain the rôle of estrogens in the ovulatory menstruation of the normal adult woman

The bleeding of estrogen deprivation does not occur if the estrogen is replaced by progesterone. After a course of progesterone, bleeding always occurs after the withdrawal of progesterone.

These experiments on monkeys and women merely established that the histologic sequences of the menstrual cycle were induced by the ovarian hormones, and that menstrual bleeding from a progravid endometrium followed cessation of progesterone action on the endometrium.

The anterior hypophysis participates indirectly in the menstrual cycle, but the work of Philip Smith shows clearly that the bleeding response to estrogens and to progesterone is not greatly changed in completely hypophysectomized monkeys.

The term "progravid" has been used to designate the histologic stage of endometrial development from the time shortly after ovulation to the cessation of active production of progesterone by the corpus luteum. All indications are that the last phase is a period of 48 hours or less which is the true premenstrual stage. It is at this stage of the cycle that attention must be focused to discover the factors which cause the hemorrhage and tissue fragmentation characteristic of menstruation.

Concomitant with the disappearance of progesterone, either in the artificial experimental cycle or in the normal cycle, several other phenomena have been clearly described by Bartelmez

The coiled endometrial arteries constrict at the base and the stroma of the endometrium becomes dehydrated. The process of dehydration is not understood but the tissue shrinks markedly. The arteriolar flow is supposed to be scanty, the pressure reduced. A peripheral ischemia ensues. This ischemia is the terminal result of the alternating "blush and blanch" arteriolar phenomena which Markee has observed in the ocular endometrial grafts. According to Markee (quoted by Bartelmez), the terminal ischemia lasts for from 4 to 24 hours.

After this, subepithelial hematomas appear, followed by their coalescence into lacunae, which begin to bleed into the lumen. Very little tissue is lost during the first 12 hours of the hemorrhage.

It is obvious that the initiation of menstruation is caused or permitted by the withdrawal of 1 or more of the hormones discussed. The hormone withdrawal theories must assume that during the interval between withdrawal of the hormone and the actual hemorrhage something happens in the tissue of the endometrium. One of the effects of this something is the constriction of the base of the endometrial coiled arteries, with the resultant ischemia. Another concomitant effect is the apparent dehydration of the stroma. The actual bleeding appears to be a result of these conditions

It appears reasonable to assume that the withdrawal of either hormone permits conditions to develop within the vascular supply or the tissue of the endometrium which leads to the phenomena of menstrual bleeding. In the case of progesterone, these changes become effective at once, after estrogen withdrawal the effect is not so localized in time, and it slowly becomes effective over a period of many days

Build, Menstrual Disorders and Obesity

L. M. Bayer¹⁵ had made anthropometric and clinical studies of 110 women and girls whose complaints were thought possibly to be associated with their build. Those with obesity or menstrual disorders or both have been omitted and 90 cases are finally considered. The dominating symptom was menstrual disorder in 46, obesity in 36, thyroid disorder in 6 and ectodermal dystrophy in 2. In an attempt to sort patients into groups according to build, various measurements, indexes and dividing limits were

tried until criteria were set up in which the photographs, the anthropometric measurements and the clinical diagnoses were in reasonable agreement.

Eventually 4 groups were defined: Feminine; hypofeminine, hyperfeminine and virile. The clinical testimony tends to corroborate the classification both in its lines of demarcation and in its developmental thesis. It has been possible to define each group not only as to build but also as to typical anatomic and physiologic corollaries.

1 In the normal feminine women the build is distinguished by normal body hair and breast development and average proportions, especially with regard to sitting height-stature and trunk-breadth indexes. Clinically these patients are usually normal except that there may be menstrual disturbances of flow and rhythm 2. The build of the hypofeminine women is distinguished by scanty body hair, small breasts, long legs and a narrow pelvis. Underweight, primary amenorrhea, incomplete genital development, delayed bone age and increased sugar tolerance constitute the associated syndrome 3 The hyperfeminine subject is distinguished by increased body hair, large breasts, short legs and a broad pelvis Overweight, advanced bone age and decreased sugar tolerance constitute the clinical syndrome Menstrual disturbances consist in irregularities of rhythm and flow 4 The build of the virile type of woman presents excessive body hair, small breasts, short legs, broad shoulders and a narrow pelvis. Overweight, muscularity, secondary amenorrhea and masculinization of the genitals constitute the extreme clinical syndrome.

Sex-endocrine Products

Clinical Uses in Gynecology—B E Urdan discusses some of the clinical uses of sex-endocrine products in various

gynecologic disorders. Amenorrhea is generally due to failure of the anterior pituitary gland or of the ovary or occasionally to failure of uterine development. Thyroid disturbances, especially hypothyroidism associated with obesity, frequently cause amenorrhea. Insufficient secretion of anterior pituitary gonadotropic substance is the commonest cause. Treatment with hypophysial extracts is the method of choice.

Estrogen is of use in amenorrhea to combat uterine atrophy and is followed by menstruation in women who have a fair degree of ovarian function. The successful endocrine treatment of most severe cases of amenorrhea will depend on the elaboration of a potent gonad stimulating product. In functional uterine bleeding there is merely an exaggerated proliferative phase of the endometrium with inadequate luteinization and thus the condition is really due to disturbed function of the anterior pituitary gland

Progestin is used in the treatment of functional hemorrhage, but the treatment is purely substitutive and the effect is temporary. In the evaluation of the problem of functional dysmenorrhea the development, the hormone control and the nervous control of the uterus must be considered along with the constitutional and nervous make-up of the individual. The property of progestin of overriding the stimulating action of estrogen would indicate its use in dysmenorrhea

Estrogen in dysmenorrhea seems indicated only in those individuals with hypoplastic uter. The most spectacular results with estrogen are obtained in patients suffering from the symptoms of the artificial or natural menopause. The author's form of therapy, with almost complete relief in all cases, is 4000 rat units of estradiol benzoate twice a week for from 4 to 8 weeks until the symptoms are controlled. This is followed by em-

tenin in doses of 1 teaspoonful daily he oral method as a rule controls paents suffering recurrences and no hyodermic medication is necessary. The range of the immature epithelium to ne adult type of vaginal mucosa and the icreased acidity of the vaginal mucosa icident to estrogen medication appear o play an important part in the eradicaon of gonorrheal vaginitis in children 'he author's method of treating senile aginitis is 2000 International Units of strogen 3 times a week for from 4 to 6 reeks. Occasionaly vaginal suppositories f estrogen are given as supplementary reatment

In functional sterility the gonad stimllating principle is best given in 2 or 3 livided doses just prior to the expected vulation Estrogen has been used in terility associated with amenorrhea, hyoomenorrhea and infantile uteri with ocasional success. However, the gonadtimulating principles are preferred. The ise of progestin in cases of habitual ibortion has a definite experimental background When avitaminosis, hypothyoidism, deficient spermatogenesis and ystemic diseases are not the causal facors in habitual abortion the use of an indocrine substance is indicated. Of the uithor's 11 patients who have had 2 or nore spontaneous abortions for which here was no apparent cause, 10 have lelivered normal infants following the ise of corpus luteum extract. The renaming patient aborted at 11 weeks One patient had a subsequent normal oirth without treatment, another was allowed to proceed in her second pregnancy without the extract but developed signs of threatened abortion which were controlled by the use of progestin Of 13 patients with threatened abortion, only 4 went to term despite the fact that reatment was instituted early. In the other 9 cases symptoms continued with

subsequent abortion Treatment in the successful cases was continued through the sixteenth week of pregnancy, 1 International Unit being given twice a week after the symptoms subsided

Pituitary Gonadotrophic Extracts for Treatment of Amenorrhea, Menorrhagia, and Sterility

R. E. Campbell and E L Sevring-haus¹⁷ report their experiences with the hypodermic administration of aqueous extracts of the anterior lobe of standardized potency. The doses employed have been 1.0 cc daily or on alternate days. These doses contained from 5 to 100 "units" each, although the definition of the unit is only roughly similar for the 3 preparations employed, i.e., prephysin, antuitrin and gonadogen.

The onset of flow, they consider, as the optimal time at which to begin use of a gonadotrophic factor when follicle stimulation was the objective Since there is increasing certainty that in a fertile 28-day cycle ovulation occurs on about the fourteenth day, they have attempted to concentrate the therapy in the first 14 days. The reason for their insistence on not using continuous injections of a potent gonadotrophic substance is that such treatment has produced follicle cysts m animals and may concervably do so in the human being. At present they prefer to remain on the side of undertreating the patient, even though they may have failures when larger doses might have produced greater success

The authors maintain that diagnoses as to the cause of amenorrhea, irregular menses, menorrhagia, and sterility cannot be made by any combination of history taking, physical examination, and pelvic examination, with ordinary laboratory tests. The use of the microscopic study of endometrium, or at times of the vaginal epithelium and the pregnandiol

excretion gives information of prime importance. Without such data diagnoses are inaccurate, and therapy is empirical. Such examinations are to precede the use of expensive and potent endocrine materials. To determine progress the history of menstrual flowing is likewise inadequate, unless fortified with similar examinations

If these aids fail to show definite response to treatment, even though menstrual flows are occurring at fairly regular intervals, the treatment may well be increased or abandoned. The use of long series of repeated daily doses, extending for 5 to 15 days at the beginning of each menstrual cycle, seems necessary and is demonstrated to be safe Results are not achieved in a single month.

Virilism in Women Caused by Androgenic Therapy for Menstrual Disturbances

J P Greenhill and S C Freed¹⁸ warn against the dangers of this drug with the introduction of testosterone propionate, an androgenic substance, in the treatment of certain menstrual disorders. This substance in doses varying from 400 to 2000 mg a month is capable of suppressing abnormal uterine bleeding At least 500 mg of testosterone propionate must be given to suppress normal menstruation. Beneficial results may be obtained with smaller doses in cases of painful breasts and dysmenorrhea. The use of testosterone propionate in these conditions was suggested by its similarity in action to progesterone. In the rat and rabbit a progestationallike state of the endometrium was induced by administration of this substance Furthermore, this androgen is capable of suppressing sex cycles of several species, inhibiting uterine contractions, neutralizing the action of estrogen on the vaginal mucosa and suppressing menstruation in monkeys and human beings, reactions typical of progesterone.

An analysis of 2 cases by the authors reveals that testosterone propionate in doses which are effective therapeutically is potent in the induction of a significant degree of virilism. Growth of hair on the face and body was stimulated and a lowering of the voice to a masculine pitch was obtained in both cases. Enlargement of the clitoris, however, was observed in only 1. It was first expected that these masculine developments would regress soon after the cessation of injections. The clitoris in the 1 case has returned to normal, but the hirsutism and male voice have persisted to the present time, 4 months after the last injection of testosterone propionate. Menstruation returned in both cases and a fibroid uterus regained its normal size in the 1 case, indicating that ovarian function returned without the disappearance of the virilism The possibility that these changes may eventually vanish is still present, but it is significant that with the removal of the masculinizing ovarian tumor, the arrhenoblastoma, the masculine voice persists, indicating that a similar result might be expected, by analogy, with the masculine voice induced by administration of androgenic substances.

At present the authors are of the opinion that androgenic therapy in women should be approached with caution and is not to be recommended until the danger of virilism can be eliminated or controlled

Low-dosage Irradiation of Pituitary Gland and Ovaries in Functional Menstrual Disorders and Sterility

C. Mazer and G Baer¹⁹ discuss the indications and contraindications to low-dosage irradiation of the pituitary gland and ovaries.

Amenorrhea and abnormal uterine bleeding, not caused by organic disease of either constitutional or local origin, in women of childbearing are amenable to low-dosage irradiation. It is also the most effective measure in the control of intractable bleeding during puberty.

An associated pelvic inflammatory condition is always a contraindication to therapeutic irradiation of the ovaries.

In view of the known deleterious effects of postconception, pelvic irradiation on the offspring, the possible presence of early pregnancy should be definitely excluded before exposing the ovaries to x-rays for the relief of amenorrhea. Moreover, in order to avoid the occurrence of conception and possible injury to the offspring during the course of roentgen ray treatment, sexual relations should be forbidden until the final treatment has been given.

Dysmenorrhea per se is only occasionally relieved by low-dosage irradiation of the pituitary gland and ovaries. Hypomenorrhea and pseudomenstruation in women with a normal menstrual rhythm are likewise refractory to this form of treatment Inasmuch as these conditions are occasionally precursors of amenorrhea, one should bear in mind that its subsequent occurrence may erroneously be attributed to such irradiation.

Technic—When ovarian hypofunction is secondary to a pituitary deficiency, such as Froehlich's syndrome, x-ray exposure of the hypophysis alone yields fairly good results. Simultaneous irradiation of the ovaries does, however, increase the percentage of cures by rendering the ovaries more responsive to the enhanced pituitary stimulation. In instances of primary ovarian deficiency, irradiation of the ovaries alone is sufficient treatment. The incidence in amenorrhea of a primary ovarian defect, totally independent of the pituitary gland,

is, however, relatively small (about 20 per cent).

The technic employed is as follows: One hundred thirty-five kv., 5 ma. at a distance of 40 cm. with 6 mm. of aluminum filtration through a field of 20 by 20 cm. The rays are directed over the anterior pelvic area Depending upon the thickness of the pelvis, 60 to 90 r. units measured in air are given to the skin This is repeated at intervals of 1 week, 3 times The total dose reaching the ovaries is about 10 per cent of a full-skin erythema. The pituitary gland is treated with the same dosage and factors through a field 3 by 3 cm. simultaneously.

Low-dosage irradiation of the pituitary gland and ovaries resulted in restoration of the menstrual function in 59 per cent of 106 cases of amenorrhea, 89 per cent of 18 cases of dysfunctional metrorrhagia during the childbearing age and in 57 per cent of 26 cases of dysfunctional menorrhagia. It had no effect in 3 cases of hypomenorrhea. The amenorrhea of 2 patients was presumably aggravated by the treatment

Low-dosage irradiation of the pituitary gland and ovaries in 26 women with normal menstrual cycles resulted in temporary amenorrhea of one who, however, had in the past shown a tendency to amenorrhea.

Nevertheless, it again points to the probability that the margin of safety in ovarian irradiation is small and that larger doses should not be employed for the present.

OVARY

Carcinoma Metastases in Ovary: Krukenberg Tumor—W Uhlmann²⁰ says that opinions are still divided regarding the nature and pathogenesis of Krukenberg tumors of the ovaries. Krukenberg considered them as primary ovarian tumors which differed from other neoplasms of the ovary by their peculiar histologic structure. The most characteristic feature of the microscopic picture of these tumors is the "signet-ring" cells, in which the nucleus is placed far to the side, as a result of the mucous transformation of the protoplasm of the epithelial cells. These cells give a positive mucicarmine reaction. Moreover, there is a considerable proliferation of the ovarian connective tissue which simulates the aspects of a fibrosarcoma and, within this tissue, the signet-ring cells appear either isolated or in groups. Krukenberg's opinion that these tumors were of a primary nature was accepted by a number of investigators, but today many observers believe that Krukenberg's tumors represent metastases of primary tumors of the intestinal tract

In this paper Uhlmann presents a statistical review of 52 of the cases of ovarian carcinoma, which were examined at the pathologic institute of the University of Erlangen In 22 of the cases the ovarian tumors were definitely of the Krukenberg type. In 11 other cases the tumors were probably also of this type, although the characteristic formation of mucus was absent. Among the 22 cases in which the ovarian tumors were definitely of the Krukenberg type there were 15 in which the Krukenberg tumors represented metastases of a primary tumor in the gastrointestinal tract. However, a primary carcinoma of the gall-bladder was detected in none of these cases Of the remaining 7 cases, only 1 can be designated as a primary tumor on the basis of post-mortem studies. In the other 6 cases clarification was impossible, because no post-mortem exammation was made. In 6 cases the appearance of the Krukenberg tumors was preceded by gastric resection on account

of carcinoma of the stomach. In 5 instances the primary tumor was detected at the time of operation.

The average age of all women with ovarian carcinoma was 46.7 years, that of those with Krukenberg tumors 45.2 years. Most of the women were of the age group between 41 and 50, but there were also some between the ages of 21 and 30. Signs of masculation were observed in only one of the women with Krukenberg tumors. In the last part of his report the author relates a case that he observed recently. This case is noteworthy because the tumor seems to be of a primary nature. Thus, of a total number of 23 cases of Krukenberg tumor, 2 may be regarded as having developed in the ovary as primary tumors, a possibility that is doubted by some investigators.

Evaluation of Ovarian Sterilization for Breast Cancer—G W. Taylor²¹ reports his experience with ovarian radiation in cases of carcinoma of the breast with bone metastases and in addition employed the procedure prophylactically after radical mastectomy in young women

These patients varied greatly on admission in the extent and stage of the disease Many were advanced, untreated cases; others presented lesions otherwise operable in whom x-ray examination detected early metastatic involvement; still others represented recurrent disease locally or metastatically, after radical or subradical surgery. It is difficult to reduce such a group to a common basis for analysis Twenty patients showed possible or probable benefit from the procedure. In many cases, when the focus of disease could be radiated, the regression may have been due in part to the local radiation rather than to the menopause. This applies particularly to recurrent nodules in the operative area, or to

supraclavicular lymph-node metastases, in which local radiation is found to be particularly effective.

Of the entire group of 50 cases, 42 patients are dead, 1 remains untraced, and 7 are still living without evident active progress of the disease.

The author concludes that artificial menopause may be expected to result in temporary regressions or improvement in about one-third of the cases with recurrent and inoperable carcinoma of the breast. The most striking benefit appears to accrue in cases with osseous metastases. Artificial menopause, however, cannot be demonstrated as advantageous when employed as a prophylactic procedure in patients who are submitted to radical operation.

Hormone studies are thus far unable to explain why the favorable effects take place, and pathological studies are unable to predict which cases will react favorably

Surgical Treatment of Bilateral Polycystic Ovaries for Amenorrhea and Sterility-Stem and Leventhal in 1935 reported 7 cases of amenorrhea associated with bilateral polycystic ovaries in whom bilateral wedge resection was performed. A large wedge of from onehalf to two-thirds of the ovarian cortex was removed and the deeper cysts in the remaining portion of the ovary were punctured The ovary was then closed by means of a single suture of fine catgut in 2 layers, the first, a deep hemostatic stitch locked at either end, and returned as a superficial approximating suture This left an ovary of approximately normal size and appearance There was restoration of the menses in all of the 7 patients, pregnancy occurring in 5 patients, twice in 3 of them. A follow-up on 6 of the 7 patients was obtained by the present authors and appears in the history abstracts above.

In the present communication I. F. Stein and M. R. Cohen²² add to this group 21 patients, all of whom complained of amenorrhea and/or sterility, and in whom bilateral ovarian enlargement was either found by palpation or demonstrated by pneumoroentgenography The combined series consists of 10 single and 18 married women Postoperatively, regular menses were restored in 23; irregular periods occurred in 2. and follow-up was unsuccessful in 3 One single girl in the first series was subsequently married and gave birth to a child at term In addition to this case, 10 of the married group became pregnant, 4 of them twice These patients were followed to date by means of menstrual calendar records and periodic pelvic examinations. No recurrence of cystic ovaries was detectable upon postoperative and follow-up examination in any case, 7 patients having been followed for more than 5 years (3, 5 years, 3, 8 years, 1, 9 years)

It would be desirable for scientific purposes to substantiate, by follow-up, the bimanual findings with pneumoroent-genograms as was done preoperatively. However, as these patients were all in good health, menstruating regularly, many of them having borne children, there was no justification from the standpoint of the patient for the additional expense and inconvenience. All of these patients are now in good health and calendar records of their menses are recorded in the case histories above.

Many surgeons are accustomed to treating polycystic ovaries incidentally found at laparatomy by multiple puncture of the follicle cysts. In 1938, Zondek advocated the performance of such multiple puncture through the culde-sac, thus obviating the necessity for laparotomy. He reported success with 40 cases.

Although 4 separate surgical methods of treating polycystic ovaries have been described, it is noteworthy, state the authors, that success in restoring the physiologic function of the ovary was obtained in each It is obvious that the good results were due to the removal of cortical follicle cysts—the significant lesion in the relationship between polycystic ovaries and the dysfunction. While the methods varied, the results were uniformly good In their opinion, Zondek's cul-dc-sac puncture of the follicle cysts appears to be too inadequate and uncontrolled for general use The procedures of both Bailey and Reycraft, based on the assumption that the thick tunica is the significant barrier to ovulation, leave the ovaries denuded of their normal epithelium, thus inviting postoperative bleeding and adhesions On the other hand, wedge resection and suture is a complete surgical technic which restores the normal anatomy of the ovary Contrary to a common prejudice, this operation is not followed by recurrence

STERILITY

Gynecological Factors—Certain aspects of sterility in which the female is entirely at fault are discussed by A. D. Campbell.^{2,3}

It is probably common experience that about one-third of all cases of so-called female sterility display no detectable lesion in the pelvis. There are in this group of cases 3 main causes for the sterility which they manifest. In the first place, there may be no ovulation, in the second place, the liberated ova may be unable to find their way into and through the fallopian tubes, and in the third place, the condition of the reproductive tract in general, and of the endometrium in particular, may be inimical to fertilization,

or perhaps more often to the maintenance and implantation of the fertilized ovum and the embryo.

Occlusion of the fallopian tubes is often due to some mild inflammatory process It should be borne in mind that peritoneal reaction as a result, for example, or regurgitation of blood through the tubes in certain cases of abortion. or of irritation of a chemical nature caused by high-pressure douches, or even ordinary soapsuds douches, may lead to the production of occluding lesions which are not palpable. Tuberculosis must always be borne in mind, not only as a possible cause of sterility, but because of the appalling risks with which it invests procedures otherwise comparatively safe.

The author points out that even when sterility is actually due to tubal occlusion, or in more general terms to failure of the ova to attain the uterus, it is not necessarily futile to attack the problem by endocrinological methods

Kaufman and others have shown that the administration of *estrin* not only causes the tubal musculature to develop, but actually leads to an enlargement of the lumen and development of the cilia

After the menopause, with the gradual cessation of production of estrogenic hormone, there is a marked impairment of activity of musculature of the fallopian tubes and gradual disappearance of the regular rhythmic tubal peristalsis Coincident with the impairment in tubal contractility the vaginal smears exhibit signs of various degrees of estrin deficiency. The most marked deficiency is seen in those patients showing least tubal activity Administration of estrin results in the development of rhythmic contraction waves of high amplitude, similar to those observed in normal females Simultaneously with the reappearance of tubal contraction, the vaginal smears

show the full effects of estrin upon the mucosa. This excellent experimental study seems to justify the impression that impairment of tubal contractility, due to estrin deficiency, may play a rôle in some form of sterility and tubal pregnancy.

It is also clear that deviation from normal in the endometrium may seriously affect the fertilized ovum before, as well as after, implantation. Since insemination will, only rarely, take place at the very hour when the ovum awaits fertilization, it is most important that the female tract should be hospitable to the sperms. The presence of infection not only in the vagina but in the cervical canal is immical to the life of the sperm Such infection may not give rise to purulent discharge, but pathogenic and pyogenic organisms in the vagina have been said to be responsible for some 50 per cent of cases of sterility. Endometritis following the use of the stem pessary is an infection contributing to unsuccessful insemination.

In Campbell's experience it is exceptional for a woman whose cycles are shorter than 27 days to become pregnant, it may be that fertilization occurs, but the embryo is aborted on the twentyseventh day, not having become firmly established before luteal function regressed. The length of the cycle depends upon the complex interactions between the ovary and the anterior pituitary, for, while the anterior lobe hormones determine follicular maturation and the formation of corpora lutea, the hypophysis is itself influenced by the hormones produced by the developing follicle and also by the hormone of the corpus luteum If any link in this chain of stimulation and inhibition is weak, it may well happen that the corpus luteum cannot of its own pituitary-controlled vitality sustain the endometrium until the twenty-eighth

day of the cycle; until the time, that is, when the corpus luteum may be reactivated and vitalized by prolan produced by the developing and implanted embryo. In such cases, the outlook becomes more hopeful if it is found possible to increase the length of the interval; even if only an occasional cycle reaches the desired length, there is always hope that a pregnancy may be successfully established on 1 of these favorable occasions.

Special attention should be drawn to the most helpful and extremely important work of Venning and Browne. They have established a relatively simple chemical procedure for measuring the quantity of pregnandiol excreted in the urine, since pregnandiol is apparently the inactive excretion form of progesterone, the hormone of the corpus luteum, this makes it possible to determine, without too much difficulty, the time when the corpus luteum begins to function as an endocrine organ, i.e., just after ovulations, and to form some estimate of its activity and vigor throughout its active life. Thus, in a patient in whom pregnandiol constantly appears at some time other than the fourteenth day of the cycle, one may recommend coitus at or about the time thus indicated. Again, a decreased pregnandiol output in early pregnancy may be regarded as a warning of a threatening abortion, which can possibly be averted by administration of appropriate amounts of progesterone.

It is well to observe here that when women who have previously appeared sterile become pregnant spontaneously, they show a considerable tendency to abort; and this is true also of women who become pregnant during treatment

Effect of Alkaline Vaginal Douche on the Huhner Test and Sterility— The effect of the alkaline douche has usually been given as First, neutralizing the acid vaginal secretions; and second, dissolving the mucous plug from the cervix. A third and possibly more important effect described by J. M. Singleton and J. L. Hunter²⁴ may be the control of the pH titer in a range which favors the lytic action of the semen on the cervical mucus, the existence of which with its variations has been demonstrated by Kurzrok and Miller.

These investigators use routinely a 24 per cent sodium bicarbonate irrigation 15 minutes before coitus in all cases where the first Huhner test shows feebly motile sperm, dead sperm, or no sperm. The irrigation is taken in the recumbent position at low pressure, and the patient is advised to move about in the erect posture immediately afterward so that the excess of retained solution may drain away. It is believed that by using this solution, after dilution with cervicovaginal and prostatovesicular secretions, an isotonic or nearly isotonic medium is obtained. The time of examination is from $1\frac{1}{2}$ to 2 hours after coitus

In the past 3 years since the institution of this procedure, 29 cases showed unsatisfactory findings with the first and satisfactory or improved with the second Huhner test. Eight pregnancies have resulted with the continuation of the alkaline douche measure,

It is pointed out that the 24 per cent sodium bicarbonate douche created a temporary incompatibility in 2 cases and the desirability of the double Huhner examination both with and without the preparatory douche, before recommending its use, is emphasized. The advisability of substituting the second Huhner test with a preparatory douche for the examination of the condom specimen, and the avoidance of further examination or treatment, medical or surgical, of the patient until potency of the husband and compatibility are established is suggested.

A very limited study of the cervical and vaginal pH under varying circumstances is presented and would indicate that the alkaline preparatory douche is ordinarily not harmful to normally alkaline sperm and is beneficial to sperm not sufficiently alkaline to overcome vaginal acidity or hyperacidity.

Sperm Examination — The importance of sperm examination in the study of a sterile mating is again emphasized by O. J. Pollák and C A. Joël.²⁵ The author points out that there are 3 conditions to be observed in investigation of the sperm:

- 1 The examination should be preceded by a pause in ejaculation of from 4 to 7 days at least Only 1 ejaculation should take place in order to provide material for examination
- 2 The material should if possible be obtained by the physician through auto-erotic manipulation or coitus interruptus. The contents of the condom are unsuitable, and other ways of obtaining material are inadequate.
- 3 The material should be examined within 30 to 60 minutes Graduated vials are suitable for eventual transport. The material is to be protected against high temperatures.

In macroscopic examination of the ejaculate, the following data are observed:

- 1. The quantity, which normally amounts to from 3 to 5 cc (average, 3 3 cc). Smaller quantities (about 0.5 cc.) usually are pathologic, whereas larger ones are not.
- 2 The consistency of the fresh ejaculate This is of a specially gelatinous character but when exposed to fresh air changes in from 10 to 30 minutes. The partly liquefied, somewhat slimy fibrous ejaculate containing white flakes is then examined. An originally thin ejaculate is usually poor in semen fibers, whereas a thick ejaculate, which does not liquefy readily, often is pathologic.
- 3 Color and smell. These will be noticed only in pathologic specimens

The microscopic investigation is actually more important. The ejaculate is well mixed with a fine glass capillary tube and a drop put on an object-bearer

If no sperms are found after repeated examination, the ejaculate should be thoroughly centrifuged.

To determine the number of sperms, the ejaculate is mixed thoroughly by means of a capillary tube and drawn up to the 005 mark of an erythrocyte-mixing pipet. A diluting fluid is then drawn up to the 101 mark, the most suitable fluid being physiologic solution of sodium chloride to which has been added carbolfuchsin 0.1 cc to 100 cc. The mixture is well shaken and a Thoma-Zeiss counting chamber filled The counting is repeated twice in order to obtain results as accurate as possible. Sixteen large squares (i c, $16 \times 16 = 256$ small squares) are to be counted In the calculation we divide by 256 to obtain the number to a small square, multiply according to the dilution by 200 and according to the chamber measures by 400,000 (1 small square amounts to 0 0025 cu mm. and the chamber depth to 0.1 mm) The formula is now. $n \times 200 \times 400,000/256 = m$ (n is the number of sperms to 16 large squares and m is the number of sperms per cubic centimeter) Normally, the number of sperms in 1 cc varies between 60 and 120 millions Higher numbers (hypersperma) are generally not pathologic, and lower numbers (hypospermia or oligospermia) are detrimental to the prognosis

The number of motile sperms is determined by means of the Ehrlich ocular screen, which divides the field of vision into 4 quadrants. Given the aforementioned conditions, especially when examination takes place within 30 to 60 minutes after the material is obtained, normally at least 80 per cent of all semen fibers are motile.

When no motile sperms are found, the authors try to call forth motility with

isotonic solutions of magnesium salts. The examination of original preparations is followed by the examination of colored smears. Colored smears are the most suitable for the differentiation of structures of sperms and of cells of spermiogenesis.

The preparations are then examined by means of immersion, and at least 200 sperms and cells are counted. Normal ejaculates have 80 per cent of morphologically normal sperms and thus at the most 20 per cent of abnormal ones. The normal relation is from 0.25 to 2 cells of spermiogenesis to 100 ripe sperms.

With this method of examination it is possible to distinguish between azoospermia and aspermia, to limit the expressions necrospermia and asthenospermia, and to establish various diseases such as localized degenerative-regenerative processes in the testicle, testicular atrophy, testicular hypoplasia, abnormalities of the epididymis, especially after gonorrhea, and, finally, derangements in the distal part of the seminal-urinary tract. Thus it is possible to form a reliable opinion about the fecundity of a man

Treatment—Between August, 1937, and June, 1938, 62 women who attended an outpatient department for sterility were observed and treated by M. M. White 26 Forty-seven of them complained of absolute sterility, 9 of 1 child sterility, 1 that she could not become pregnant with a second husband (although she had had 4 children by the first husband) and 5 that they had had 1 or more miscarriages. By September, 1938, 22 patients were pregnant—that is, 478 per cent of those in whom pregnancy was possible, since 16 patients either had nonpatent fallopian tubes or their husbands were known to be sterile Of the 22 who became pregnant, 7 miscarried, but 2 are now pregnant again.

Of the remaining 24 women who have not yet become pregnant it is assumed that in 21 per cent the husband is sterile, judging from the result of the 39 whose semen was examined; but this still leaves a number of women in whom so far pregnancy has not occurred though study of both partners has been favorable.

Iodized poppyseed oil by itself has a therapeutic value in that it opens the fallopian tubes. It would seem to be of greater use than air insufflation, because the latter ceases to distend as soon as the pressure is reduced. Forty patients injected with the oil received no glandular therapy and 13 became pregnant There was tubal occlusion or sterility of the husband in 14 of these 40 cases, so that a 50 per cent success can be attributed to the injection of the oil alone. It is known that the failure of many patients to conceive is due to failure of ovulation, and it is claimed that ovulation is more likely to occur after suitable administration of endocrine products

Dihydroxyestrin benzoate given in 2 weekly doses of 20,000 international benzoate units in the 2 weeks directly following the menstrual period, or as a larger dose of 50,000 international benzoate units about the twelfth day of the menstrual cycle, appears to have had some value. In cases in which the uterus is undersized, indation of the fertilized ovum is more likely to occur if further development is brought by more regular and prolonged glandular therapy. Failure of the fertilized ovum to embed is one of the causes of sterility.

Investigation on the pregnandiol (excretion product derived from the corpus luteum) content in the urine at the time of ovulation in sterile patients is being undertaken. Insufficiency of the latter substance may be dependent on an insufficiency or an unbalanced output of anterior pituitary hormones.

STILBESTROL

Two new compounds—ethinyl estradiol and diethylstilbestrol - have been used clinically in recent months and have been shown to be as effective as the injected estrogens in moderate doses. General acceptance of these compounds has been prevented by complaints of disagreeable symptoms following their ingestion. Ethinyl estradiol induced in a considerable percentage of patients nausea, vomiting, headache, and malaise Diethylstilbestrol, however, has been prescribed, especially in England. The reports as to the toxic reactions of this substance are quite conflicting, some investigators stating that gastric distress is the only complaint, that this is experienced by from 5 to 10 per cent of the patients, and that it vanishes after a few days of administration Others have found side reactions in greater numbers.

Properties of a Synthetic Estrogen-P M F Bishop, M. Boycott and S Zuckerman²⁷ administered a synthetic estrogen (stilbestrol) to 18 patients with amenorrhea of variable duration "Estrogenic withdrawal bleeding" was provoked in 8, and rhythmic uterine hemorrhage occurred during the period of administration in 2 Of the patients who did not respond by uterine bleeding, 1 had previously failed to respond to the administration of natural estrogens and 1 had received no previous therapy. The amenorrhea in this patient was of 8 years' duration, the onset having accompanied that of anorexia nervosa. Six patients failed to respond to the synthetic estrogen though previous courses of theelol (estradiol benzoate) had resulted in withdrawal bleeding Of the 10 treated successfully, 3 had received no estrogen previously but responded to such low doses as 14 mg. or less given by mouth

In 15 patients with the menopausal syndrome, and in 10 with atrophic con-

ditions of the vagina, symptomatic relief (especially with regard to the daily frequency of hot flushes), vaginal smear pictures and improvement of the local condition (of the vagina) were taken as the main criteria of response. Of these 25 patients, 8 failed to respond to the administration of the synthetic substance Five of these received relatively small doses, totaling 2.8 mg or less, though 3 of these had reacted satisfactorily to lower doses of ethinyl estradiol (a partially synthetic compound of natural estrogen). Of the remaining 3, 2 were suffering from atrophic vaginitis, neither had received previous estrogenic therapy and with both there was doubt as to whether the local condition was due to ovarian deficiency The third patient failed to react to small doses of ethinyl estradiol. Of the successfully treated patients 1 reacted to 01 mg given by mouth daily for a fortnight both symptomatically and with the production of an estrous smear (though the improvement was not maintained after a further course) Another patient failed to respond to doses of 0.1 mg but reacted satisfactorily to 1 mg doses both as to the fortnightly hot flushes and the vaginal smear. In all the other subjects doses of 1 mg or more produced satisfactory responses

Symptomatic improvement was almost always associated with a transformation of the vaginal smear to the estrous type. Two patients with dysmenorrhea were completely relieved by the daily administration of 1 mg tablets of the synthetic substance during the first half of the cycle. They had experienced similar relief from 4 injections of 5 mg of estradiol benzoate. Nausea or vomiting occurred in 3 cases. The authors do not believe that these symptoms depend on dose given.

Stilbestrol and Anhydro-oxyprogesterone in Menstruation and Lac-

tation—R. Wenner and K. Joel²⁸ report the results on their study of (1) the minimal dose of stilbestrol necessary to produce proliferation in a resting or atrophic endometrium, (2) the dose necessary to induce a hyperproliferation (in the sense of glandular cystic hyperplasia), and (3) the doses necessary to prevent and to inhibit lactation in the puerperium At the same time they tried to ascertain the oral dose of corpus luteum hormone (anhydro-oxyprogesterone) necessary to produce the stage of transformation of the endometrium with subsequent menstruation

The authors studied the effect of stilbesterol and of anhydro-oxyprogesterone on the endometrium of 1 woman who had attained the climacteric 13 years earlier and on 8 women who had been castrated by means of roentgen treatments 2 or 3 years previously, when they were over 45 years of age. Each woman was subjected to 3 curettages, 1 before treatment was begun, the second after the administration of stilbestrol and the third after treatment with anhydro-oxyprogesterone. They found that in order to obtain proliferation of a resting or atrophic endometrium, it is necessary to give 25 mg of stilbestrol by mouth or 15 mg by intramuscular injection from 50 to 60 mg of stilbestrol are given by mouth, a glandular cystic hyperplasia can be produced. The stage of transformation and the menstruation following proliferation can be produced by the oral administration of from 220 to 300 mg of anhydro-oxyprogesterone In only 2 cases did the administration of stilbesterol cause slight secondary symptoms, and even these disappeared rapidly In the second part of this report, the authors describe their studies on the effects of stilbestrol on lactation several investigators had succeeded in either preventing the influx of milk of

inhibiting lactation by the administration of estrogenic hormone, the authors decided to use stilbestrol for the same purpose. In 6 cases (4 stillbirths, 1 case of tuberculosis, and 1 of depressed nipples) they administered stilbestrol on the first day after confinement to prevent the secretion of milk. In 3 of these cases, 1 tablet (5 mg.) was given and in the other 3, 2 tablets (10 mg.) The treatment was successful in all of these cases; no milk was secreted, and the breasts remained flaccid. In 14 cases stilbestrol was given to inhibit established lactation, the indications being hypogalactia, bleeding fissures, mastitis, eczema of the breasts, and tuberculosis It was found that to arrest lactation, from 5 to 10 mg of stilbestrol are usually effective, but in some cases larger doses are necessary (not more than 20 mg.)

Stilbestrols in Ovarian Insufficiency—H Tuscher²⁹ thought it advisable to study the activity of the synthetic estrogenic substances not only in cases in which ovarian insufficiency was brought on by surgical removal or physiologic involution of the ovaries but also in those cases of ovarian insufficiency which appeared in comparatively young women, for instance, after a pregnancy women may complain of cessation or of rare or scanty menstruation, of increase in weight, of hot flushes, and so on, that is, of signs that are characteristic of the physiologic menopause. Instead of employing the natural female sex hormone, it was decided to employ the stilbestrols, namely, the diethylstilbestrol diproprionate and the diethylstilbestrol In addition to a number of women with ovarian dysfunction of unknown etiology, the author treated 8 women with secondary amenorrhea or hypomenorrhea after pregnancy

The exclusive administration of stilbestrol may bring on the menstrual flow and regulate the cycle In cases in which the administration of the stilbestrol did not induce menstruation or in which the effect was only temporary, corpus luteum hormone was given. The dose of stilbestrol was not increased, in order to avoid excessive doses and undesirable effects. such as vomiting. The author advises that treatment be initiated during the proliferative phase with 1 cc. (0.5 mg) of the diethylstilbestrol diproprionate or with 1 cc. (075 mg.) of diethylstilbestrol diacetate This dose is given every second or third day for a period of 2 weeks. If there is no result or if the menstruation is weak, the same series of treatment can be repeated 2 or 3 times, if necessary, with the aid of the corpus luteum hormone during the second half of the intermenstrual period. The author advises against an increase in the individual dose of stilbestrol. The results that are obtained with the stilbestrols indicate that although they differ from the natural female sex hormones in chemical structure they nevertheless exert the same biologic action They are well tolerated when given in correct doses.

Effects of the Therapeutic Use of Diethylstilbestrol—The possibility that the substance may have further toxic effects on the liver, kidney, or hematopoietic system has led to the investigation of 17 cases by C. L. Buxton and E. T. Engle, 30 in which varying doses of stilbestrol were administered. In these cases the following diagnostic procedures were carried out. Complete blood counts, including platelets, urinallysis, serum protein partition, icteric index, and the van den Bergh reaction.

No persons were treated who had a family history of mammary carcinoma

The dosage of stilbestrol varied greatly, some patients receiving as little as 1 mg a day for 1 week and others as much as 30 mg a day for from 14 to 21 days

One patient received 1320 mg. over a period of 4 months. Improvement of symptoms had no relationship to the amount of medication given, 1 mg a day having been found sufficient in some cases whereas as much as 30 mg a day for 20 days was of no help in others.

Patients with kraurosis vulvae, leukoplakia and senile vaginitis were grouped under the latter heading for the sake of convenience. They received stilbestrol in the form of wool fat outment. All reported relief of symptoms, and the appearance of the local lesions improved.

As far as can be ascertained from these laboratory studies, no evidence of toxicity can be attributed to this estrogen in 16 of 17 cases treated. Toxicity possibly attributed to this substance was observed in 1 patient with positive urinary manifestations. There has been no evidence of allergic or urticarial phenomena.

The nausea and vomiting is not thought to be a contraindication to the use of stilbestrol. These symptoms may be partially avoided by the use of gelatin capsules.

The actions of estrogens in any or all species of animals, in causing squamous cell metaplasia of both genital and extragenital tissues, of a direct effect on the anterior pituitary gland and other less definite but alleged effects have not been as yet clearly demonstrated in the human being. However, the observed effects in women and the abundance of data on progressive effects in animals should raise a reasonable doubt in the mind of the clinician that these substances may be given with impunity

UROLOGICAL CONDITIONS

Differential Diagnosis — Problems in differential diagnosis between uro-

logic and abdominal lesions are discussed by H. L. Kretschmer.³¹

1 Lesions of the Gastrointestinal Tract—Lesions of the gastrointestinal tract probably constitute the largest group that calls for differentiation and, of these, appendicitis heads the list. The differentiation between lesions of the urinary tract and lesions of the appendix should be relatively simple; however, the large number of patients seen by the urologist each year for the relief of urinary symptoms, in whom an appendectomy has failed to effect a cure, is evidence that the differentiation is not made as frequently as it should be

At times the differentiation between acute appendicitis and acute pyelitis is difficult, especially if a patient with an acute disease of the appendix has some red blood cells and perhaps a few pus cells in the urine and it is difficult to obtain an accurate history. In a child having acute, severe pyelitis with rightsided pain and tenderness, the differentiation is especially difficult if the urmary findings are negative, as they may be during the first 24 or 36 hours, after the urine becomes loaded with pus, the diagnosis is self-evident. The number of cases in which this differentiation is impossible and in whom it is necessary to perform an appendectomy is very small indeed

This differentiation may present great difficulties in an adult female who has had severe attacks of pyelitis during 1 or more pregnancies. If a woman who has previously had attacks of pyelitis suddenly develops an attack of acute appendicitis, it is easy to understand why the attack of appendicitis may be overlooked and the clinical picture attributed to a lighting up of an old infection in the kidney. In this type of case, if after due deliberation and consultation, it is not possible to make the differen-

tiation, one should give the patient the benefit of the doubt and operate on her rather than run the danger of overlooking an acute appendix and having the patient die of generalized peritonitis.

- 2 Lesions of the Gall-bladder— The problems of differential diagnosis between lesions of the gall-bladder and the kidney, has become greatly simplified since the advent of pyelography and cholecystography.
- 3 Subphrenic Abscess Following Pregnancy—Although the occurrence of chills and fever, the presence of pain in the right kidney area, and pus in the urine occurring during pregnancy would seem to justify the diagnosis of pyelitis of pregnancy, one must always be on the alert for the possibility of some lesion outside the urinary tract such as subphrenic abscess that may be responsible for the clinical picture that may occur during pregnancy or the puerperium.
- 4 Cyst of the Pancreas—As a general premise, one may state that cysts of the pancreas are rare and present no pathognomonic symptoms Physical exammation reveals an elastic swelling in the epigastrium, generally in the midline The onset is slow and the nature of the disease is progressive. In the majority of cases the swelling comes forward so that it is readily palpable. Displacement of viscera may occur and, in rare instances, there may be displacement of the kidney Cysts of the pancreas may be confused with lesions of the kidney, such as hydronephrosis and tumor, especially when there is some displacement of the kidney
- 5 Lesions of the Colon Lesions of the large bowel are of interest to the urologist because some of them may result in the production of enterovesical fistulas. The 2 lesions most frequently responsible for the production of the fistulas are diverticulitis and carcinoma.

Simple, or so-called self-limiting, diverticulitis may produce bladder symptoms occasionally and hence be the subject for differential diagnosis. When the inflammatory process extends beyond the wall of the diverticulum, peridiverticulitis with abscess formation occurs. The abscess may rupture into the bladder, either with or without the formation of an enterovesical fistula

- 6. Acute Pyelitis Following Operation—During the postoperative course following a major surgical operation, symptoms and signs may develop that are difficult to interpret and evaluate: (1) The clinical picture may be due to a lesion not recognized before operation and yet part of the primary pathology for which the patient was operated upon. (2) The clinical picture may be due to a lesion of the urmary tract, which, because of the absence of symptoms and signs was not recognized before operation, for instance, the presence of a stone in the kidney or ureter, but following operation an acute pyelitis develops and the true condition in the urinary tract is then recognized (3) A combination of symptoms that may be due in part to both conditions
- 7. Lesions of the Gynecological Tract—Various pathological conditions in the gynecological tract are often the cause of urmary symptoms. On the other hand, in some cases the patient may have disease in the urinary tract that is the direct cause of urmary symptoms, and with it may be associated conditions in the gynecological tract, such as prolapse of the uterus, cytocele, rectocele, fibroid, and various lesions of the tubes and ovaries. It is not at all an infrequent occurrence to see a patient in whom the urinary symptoms are erroneously attributed to the pelvic disease and for which the patient is operated upon without relief of the urinary symptoms Among

some of the more frequently overlooked lesions may be mentioned chronic pyelonephritis, hydronephrosis, renal and ureteral stone, renal tuberculosis, and elusive ulcer of the bladder. Just as the gynecologist should bear in mind the fact that his patient may also have a lesion in the urinary tract, so must the urologist bear in mind that his patient's symptoms may be due to a lesion in the gynecological tract

- 8 Lesions of the Spine Because of the fact that pain in the back is not always of renal origin, it is necessary that the urologist, in his consideration of differential diagnosis, bear in mind the fact that the patient may have a lesion of the spinal column, i c, (1) arthritis; (2) lesions of the vertebrae, and (3) prolapse of the nuclear pulp.
- 9 Hydronephrosis—Hydronephrosis is one of the common lesions of the kidney that is frequently overlooked and confused with various intra-abdominal lesions. In some cases, there are no symptoms referable to the kidney and the hydronephrosis is discovered only upon routine examination. In other instances, the only manifestation of hydronephrosis is indefinite pain in the abdomen, the cause of which is not recognized, and, in some cases an abdominal operation is performed without relief of symptoms.

Because of the large size of the hydronephrosis, the condition may be confused with various types of intra-abdominal swellings. In another group of cases the patient may develop severe pain, which may even result in shock and collapse, so that the clinical picture is that of an acute intra-abdominal emergency

10. Retroperitoneal Tumors—It is a well-known fact that retroperitoneal tumors produce no typical clinical symptoms by means of which they can be recognized, and that, as a rule, when the patient is seen, the tumor has reached a

large size In an occasional case, the tumor is discovered after the patient has received an injury, and in other instances the only complaint is that of indefinite pain.

Retroperitoneal tumors are often confused with lesions of the kidney, adrenal, pancreas, and Riedel's lobe of the liver A complete urological study is always indicated and is most informative. Ureteral catheterization and retrograde pyelograms show 2 common findings that are of great value, namely, displacement of the kidney pelvis, with or without changes in the pyelogram, and changes in the course of the ureter

11 Elusive Ulcer—One of the lesions of the urinary tract frequently confused with lesions of the lower abdomen is the so-called elusive ulcer. This condition is relatively uncommon, yet it occurs with enough frequency to justify bearing it in mind in the differential diagnosis of lesions of the lower abdomen

The author concludes that the rôle of the urologist is a very important one in the differential of abdominal disease. He must be familiar with the various types of intraperitoneal, as well as retroperitoneal lesions that may be confused with lesions of the genitourniary tract. It is most important that he be familiar with complications that arise following general and gynecological surgical procedures.

UTERUS

Bleeding from Uterus

Production of Uterine Hemorrhage by Progesterone—B Zondek and S. Rozin³² learned that if progesterone is administered to normally menstruating women for 5 days during the postmenstrual stage (seventh to twelfth day of the cycle) bleeding of several days' duration occurs after an interval of 60 hours on the fourteenth day of the cycle. Since the uterine mucosa in this stage does not show any of the secretory stage or only the beginning of it, this hemorrhage can be looked on as pseudomenstruation. The normal ovarian cycle need not be disturbed by this event.

If progesterone is administered at the time of the follicular rupture, at a moment when the patient has her own corpus luteum, bleeding either does not occur at all or there is a hemorrhage from a mucous membrane already developed into the premenstrual stage. In this case precocious menstrual bleeding can be induced.

The authors also observed that treatment with progesterone for 5 days can produce hemorrhage in secondary amenorrhea without preliminary treatment estrogenic substance. In primary amenorrhea, however, such treatment fails. Since it had become evident that progesterone could induce hemorrhage in the normal as well as in the disturbed ovarian cycle, the authors tried to initiate hemorrhage during pregnancy in order to bring about therapeutic abortion in this way. They used doses of from 50 to 150 mg of progesterone. Bleeding, however, did not occur and pregnancy continued.

According to Zondek and Rozin, hemorrhages are produced during the intermenstrual stage in the normally menstruating women by means of parenteral administration of progesterone or the oral administration of pregneninonol (300 mg) intracyclical hemorrhage. If a woman is injected with 10 mg of progesterone daily during the postmenstrual stage, i.e., from the fifth to the minth or from the seventh to the eleventh day of the cycle, a total dosage of 50 mg, hemorrhage sets in after an interval of 60 hours, that is, on the twelfth or the fourteenth day of the cycle, and persists

for 3 to 4 days. During the period when progesterone is given, the patients notice swelling and pain in the breasts, as well as pain in the abdomen, all these symptoms subsiding as soon as the hemorrhage commences. The blood discharged in this intracyclic hemorrhage does not coagulate, a quality characteristic of true menstrual blood.

In a further investigation, B. Zondek and S. Rozin³³ observed that progesterone is not effective if given in the intermenstrual stage, *i. e.*, during, or subsequent to the rupture of the follicle, at a time, therefore, when the woman is already under the influence of the endogenously produced corpus luteum hormone. The intracyclic hemorrhage, therefore, does not occur if there is not an interval between the exogenous administration and the endogenous production of the corpus luteum hormone.

In addition, these investigators noted that the estrone level which is physiologically present during the intermenstrual stage does not prevent the intracyclic hemorrhage, if, however, additional amounts of estrogenic hormone are given, the inhibitory action becomes effective. The estrogenic hormone interferes with the hemorrhage-producing effect of the corpus luteum hormone, as well as with the gonadotrophic mechanism of the anterior pituitary.

Pregneninonol given *per os* has the same effect as has progesterone given parenterally.

Testosterone Propionate in Functional Bleeding — S. H Geist, U J Salmon and J. A. Gaines³⁴ used testosterone propionate in the treatment of 25 women with functional uterine bleeding. The bleeding was rapidly controlled in all but 2 of the cases. This improvement was correlated with definite changes in the endometrium, as revealed by suction biopsies performed at intervals be-

fore, during and after treatment. In all but 4 of the women there was no palpable organic disease; small intramural myomas were present in these 4. There were 13 cases of menorrhagia, 5 of menometrorrhagia, and 7 of menorrhagia with polymenorrhea The ages of the patients varied from 24 to 39 years. The duration of abnormal bleeding varied from 2 months to 10 years, with an average of 2 years The monthly dosage varied from 300 to 1000 mg. of testosterone propionate. The highest dosage given any single patient was 2150 mg. over a period of 3 months The testosterone propionate was administered intramuscularly in sesame oil in doses of from 5 to 100 mg. The intervals between doses are determined individually Normal menses were established in 18 cases and amenorrhea of 1 to 5 months in 5

Endometrial biopsies performed during and after the period of testosterone propionate administration revealed disappearance of the secretory phase and inhibition of the proliferative phase, often with regression to the hypoplastic or atrophic state. Following the discontinuation of therapy, the inhibitory effects on the endometrium gradually disappear and normal estrogen and progesterone effects reappear. The authors suggest that the changes in the endometrium following testosterone propionate therapy are the end results of a primary inhibition of the gonadotrophic factors of the hypophysis, causing suppression of the ovarian cycle. with consequent cessation of estrogen and progesterone production

Carcinoma of Uterine Body

Surgical and Radiation Therapy—W. P Healy and R. L. Brown³⁵ review their experience with 197 patients with carcinoma of the corpus uteri admitted to the Gynecological Service at the Me-

morial Hospital during the 15-year period from 1918 to 1932. The authors believe that whenever possible intrauterine radiation should be followed by complete abdominal hysterectomy. When there is clinical extension of carcinoma beyond the uterus, the chance for cure is slight regardless of the method of treatment employed.

The patient's history will often suggest the presence of corpus carcinoma, and if so, radon is held available in the operating room at the time, a diagnostic curettage is done. If the gross appearance of the curettings is suggestive of carcinoma. a radon tandem of 2 or 3 capsules, depending on the size of the uterus, is placed within the uterine cavity immediately after the curettage. The radon capsules are each 15 mm in length, have a combined strength of 75 to 150 millicuries, are filtered by ½ mm of platinum and are encased in a small rubber tube. the wall of which is 2 mm, thick frozen section is done to establish the diagnosis microscopically, and, if carcinoma is found, the radon is allowed to remain in place for a dose of 3600 millicurie hours. The diagnostic curettage and insertion of radium are done under The radon tandem general anesthesia is sutured in place by means of a catgut suture passed through the cervix and tied in a bow knot so that removal is not difficult. The vagina is packed with sterile gauze and a Pezzer catheter placed in the bladder. The patients are kept in bed until the radium and catheter are removed and for 3 or 4 days thereafter.

Two weeks after the intrauterine application of radon external radiation by means of 200 ky roentgen ray is given, 750 r being given to each of 4 pelvic ports 11 by 14 cm in size at a target skin distance of 70 cm milliamperage of 30, and filtration of ½ mm. copper. One

pelvic portal is treated daily or on alternate days.

Six or 10 weeks after the completion of radiation a complete abdominal hysterectomy is performed, the entire uterus including the cervix with both tubes and ovaries being removed. One of the first steps in the operation is the closure of the fimbriated ends of the fallopian tubes by ligature. Care is taken to avoid trauma to the uterus and no tenaculum or forceps is placed on the body of the uterus at any time

When the diagnosis is quite definite from history and clinical examination, it is considered advisable to give the external radiation 2 weeks before the curettage and insertion of radium. When radiation alone is to be relied upon, another curettage should be done 4 to 6 months after the first curettage or when there is any recurrence of symptoms. If residual carcinoma is found, treatment by intrauterine radon not over 2500 millicurie hours should be given

The operative mortality for the 93 patients subjected to hysterectomy following radiation therapy was 43 per cent.

The principal cause of death in the entire group of 197 cases was residual or recurrent carcinoma in the pelvis about the vaginal vault, causing hemorrhage or obstruction of the ureters with resultant Four cases had pulmonary metastases proved by x-rays, 1 of these cases had metastasis to a cervical node proved by biopsy. Two patients died of carcinoma primary in another part of the body and apparently unrelated to the corpus cancer One of these developed carcinoma of the breast 12 years after hysterectomy and died of carcinoma of the breast 2 years later The other died of squamous carcinoma of the vulva 6 years after radiation and hysterectomy for adenocarcinoma of the corpus uteri.

Endometrial Studies

W. E. Herrell³⁶ attempts to correlate endometrial studies with ovarian dysfunction and uterine malignancy.

The activity of the ovary, as is well known, is reflected in the activity of the endometrium. The normal endometrial cycle Herrell divides into the menstruating phase, a phase of early proliferation, a phase of late proliferation, a phase of early differentiation, and a phase of late differentiation. The 4 last named phases correspond roughly to the 4 weeks of the normal menstrual cycle in the order named. The abnormal endometrial cycles, which are due to abnormal ovarian activity, reflect themselves in arrest of the cycle in any of the phases named above The phase of arrest is called the persistent phase and the stage of arrest depends on the degree and kind of ovarian dysfunction.

Ovarian dysfunction can be divided into a primary and a secondary group. The primary ovarian dysfunctions are due to failure in the ovary itself. The secondary dysfunctions are due to changes in the ovary which accompany or follow failure of the thyroid or pituitary functions. In both groups the histologic manifestations are the same because, as stated, the endometrium reflects only the activity of the ovary

The study of cystic changes in the endometrium associated with different phases of the cycle indicates that one can separate to some degree the cases of sterility from those of bleeding dysfunction. When cystic changes are present in the proliferative phase of the cycle, the tendency is greatest toward bleeding dysfunction and to a lesser degree toward sterility. On the other hand, when cystic changes are associated with the differentiative phases, the tendency is greatest toward sterility, while the tendency to-

ward bleeding dysfunction is almost entirely absent.

Carcinoma occurs practically always in the proliferative type of endometrium but is an endometrium the characteristics of which result from unopposed action of estrin (folliculin) and from absence or failure of activity of the corpus luteum. Even when carcinoma of the endometrium occurs in the preclimacteric state, as it does in approximately a fourth of the cases of endometrial carcinoma, the endometrium usually is of the persistent proliferative type and only rarely is there any evidence of differentiation or of activity of the corpus luteum. The ovaries associated with fundal carcinoma contain cystic portions which probably are the source of estrin in 90 per cent of the cases of carcinoma. Further evidence in support of the view that this endometrium, in which carcinoma occurs, is attributable to the presence of the action of the estrogenic hormone, is indicated by the presence of estrin in the urine of patients whose uterine fundi harbor malignant growths. This type of endometrium is markedly different from the true atrophic endometrium which results from castration. Caremoma of the body of the uterus never has been seen. according to Herrell, if an individual has been previously castrated

It seems reasonable to conclude that the unopposed action of estrin, with its resulting effect on the endometrium, which is a persistent proliferative type of endometrium with cystic change, is the basic principle at work in the development of malignancy of the endometrium of those individuals who possess the genetic factor necessary for the development of cancer.

Prolapse

An illuminating treatise on the modern concept of the etiology and management of uterine prolapse is offered by J. L. Baer.³⁷

The present approach to the problem of prolapse of the uterus, states the author, should begin with an understanding of the formation of the urogenital tract and the ways in which defective development may predispose to prolapse of the uterus.

The development of the broad ligaments and the entire superior fascial plane parallels the completion of the female genital system. Defects in the one may result in defects in the other.

Approximately 20 per cent of adult women who are otherwise normal show a retrodisplacement of the uterus. Spina bifida occulta predisposes to prolapse of the uterus. With this lesion, there is an involvement of the cauda equina which results in an inadequate innervation of the pelvic musculature. The association of prolapse of the uterus in the virgin adult and indeed in the infant with spina bifida occulta is a well-recognized sequence.

Variations in the location of the cervix in relation to the pelvic midaxis arise from the abnormal development of the supporting plane. Most commonly the uterus is in retroversion and the cervix is near the symphysis, an abnormally short anterior fascial segment, or the entire anteflexed uterus is in retrocession, an abnormally long anterior fascial segment. Finally, there is a small group of nulliparous young women in whom the external os is within 4 centimeters of the vulvar outlet without elongation of the cervix, a descensis of the uterus

Birth injuries arising from a multitude of causes eventuate into prolapse of the interus when the integrity of the superior fascial plane is undermined. Damage to the lateral paravaginal segments is first in importance. Damage to the anterior segment of the plane determines the de-

gree of associated cystocele Damage to the uterosacral ligaments is negligible as a determining cause of prolapse. Birth injuries should be placed in 2 categories—those which are self-inflicted, and those which are chargeable to the accoucheur Tumultuous labor with too violent efforts on the part of the woman can so overstretch and traumatize the superior fascial plane as to result in an immediate dencensus of the uterus. This is particularly true of the multipara who has learned that bearing down hastens delivery and exerts her voluntary musculature against the partially dilated cervix.

The actual development of prolapse of the uterus is the result of downward pressure from within the abdominal cavity, transmitted against the uterus at its circle of attachment to the superior pelvic fascia. It is true that in the vast majority of instances the prolapsed uterus is likewise retrodisplaced. This retrodisplacement places the corpus in line with the axis of the vagina. The effect of continued downward pressure results in a gradual eversion of the vagina, accelerated by the piston effect of the corpus uteri just above it

Destruction of the anterior plane of fascia results in cystocele. Studies of cystocele have indicated that this lesion should be divided into 2 groups—those in which the urethra and vesical sphincter retain their normal relation while the floor of the bladder is dislocated downward into the anterior forms, and those in which the trigone, vesical sphincter, and urethra participate in the hermation

The pelvic floor, which includes particularly the levators and their covering fasciae and the perineal body, plays no rôle in the development of prolapse of the uterus. In the surgical treatment of prolapse, however, an adequate pelvic floor is an important factor in establishing a cure.

Treatment — The treatment of prolapse of the uterus is essentially surgical.

In the childbearing woman who wishes to remain fertile, Baer elects the modified *Fothergill parametrial fixation*, sometimes known as the *Manchester operation*.

This operation, besides conserving the uterus, restores it to normal length and anteplacement, including an adequate cervix, accomplishes a reconstruction of the anterior vaginal wall and the correction of the bladder herma, and finally includes the restoration of the pelvic floor, which is important in the success of the operation

He chooses the Watkins interposition operation for the woman at or near the menopause in whom the uterus is normal, neither too large, nor too small, freely movable, with no adnexal pathology, and especially in whom there is a large cystocele. This is ideal for support of the bladder, and for a successful outcome requires only that the fundus uteri be properly anchored under the subpubic angle, that excess cervix be amputated, and that an appropriate posterior vaginal reconstruction be done. If there is the possibility of pregnancy, sterilization must be added. He prefers the Walthardt modification of the Madlener tubal ligation to cornual excision

Baer uses the Mayo type of vaginal hysterectomy in the presence of intrinsic uterine pathology. Overly long broad ligaments should be imbricated. In vaginal hysterectomy it is vital that the vaginal vault be firmly anchored lest a vaginal prolapse occur subsequently. For this, uterosacral ligaments and bases of the broad ligaments are utilized. He does the usual anterior and posterior colporrhaphy, closing the vaginal vault transversely with interrupted sutures, and does not employ drainage.

The Neugebauer-LeFort occlusion operation, or colpoclessis, is ideal in the older woman in whom marital relations no longer exist and in whom the uterus is usually atrophic. In this operation it is important that the anterior denudation stop 3 to 4 cm. away from the external urinary meatus, lest the drag of the approximated perineal body result in a subsequent vesical impairment or incontinence.

When the indications for the Neugebauer-LeFort colpoclessis are present, but marital relations must still be provided for, Goodall has suggested an occlusion of the upper half of the vagina. If this provision were inadequate, and the patient's condition did not warrant the prolonged vaginal procedure, Baer then has recourse to the Kocher-Murphy extrafascial abdominal fixation operation.

The occasional instance of prolapse of the vagina can best be handled by a complete colpectomy. If marital relations must be conserved, Baer would select the Brady vaginal abdominal fixation operation.

In patients in whom the uterus is preserved, it is important to reduce the over-all length of this organ to about 8 centimeters by amputation of the cervix. At the same time it is important to do a diagnostic curettage. Posterior reconstruction must be adjusted to avoid too tight an introitus and yet provide thorough levator reconstruction where this muscle sling has been partly traumatized or is atrophic.

Palliative Treatment—There is a group of patients in whom surgical cure cannot be carried out (1) Those who refuse surgery, (2) those whose general condition is such as to make surgery a prohibitive jeopardy; (3) those in whom complications require treatment before surgery can be undertaken

and who must be relieved temporarily, and (4) those in whom pregnancy is associated with prolapse.

For women who require permanent palliative treatment, various *pessaries* have been devised. These usually depend for their efficacy upon the presence of a sufficiently good pelvic floor to provide a support for the pessary which in turn carries the prolapsed uterus.

The inflatable rubber doughnut pessary has largely displaced the ball pes-This likewise is obtainable in various sizes and is the most comfortable and most satisfactory of the available devices It tends to deflate slowly and the surface gradually becomes granu-This type should be removed lar. monthly, the vaginal walls inspected for decubitus, and the pessary itself examined for deterioration. It usually requires some reinflation, which can be done with a fine needle (26 gauge) and a 10 cc. The patient, when properly fitted, should have no sense of discomfort nor an awareness of its presence Gellhorn pessary, obtainable in 2 sizes, serves very well when the doughnut pessary is not tolerated because of bladder pressure

For the woman who cannot tolerate self-retaining pessaries because of pressure on the adjacent viscera, the cup and stem instrument, such as Mackintosh, is available. This holds the prolapsed cervix in a small, vulcanite, saucerlike cup, which in turn rests on a heavy, semi-flexible stem which protrudes from the vulva. At the outer end there are 2 perforations through which rubber straps are passed which are secured front and back to an abdominal belt.

For the *pregnant woman* with prolapse, the ideal treatment is **rest** without the use of any mechanical devices Usually after mid-pregnancy, the ab-

dominal mass serves to reduce the degree of prolapse.

Retrodisplacements

Treatment — This is discussed by W. T. Dannreuther.³⁸ A retrodisplacement may be treated prophylactically, expectantly, palliatively or surgically. Proper precautionary measures following abortion, labor and vaginal operations involving traction on the cervix will prevent many acquired malpositions After therapeutic abortion, packing the uterus with iodoform gauze for 48 hours and administration of 1 cc. of solution of posterior pituitary twice daily for 3 days will hasten involution After delivery, perineal lacerations should be repaired immediately to restore the integrity of the perineal musculature. Elevation of the patient's shoulders on the second day promotes free lochial drainage Assuming the prone position for 5 or 10 minutes several times each subsequent day facilitates forward gravitation of the uterus and exertion of the intra-abdominal pressure on the proper Deep breathing exerfundal area cises in the knee-chest position during the third and fourth postpartum weeks help to prevent diastasis of the abdominal muscles and also tend to throw the corpus forward

Regular and continued breast feedings reflexly stimulate pelvic involution and should be urged for this as well as other reasons. If all patients are reexamined 3, 6 and 12 weeks after abortion or parturition, retrodisplacements will be detected promptly

It is axiomatic that the farther back the cervix, the farther forward the corpus. Hence the importance of replacing the uterus bimanually and holding the cervix back in the pelvis with a strip gauze vaginal pack, pressed firmly against the portio, after operations such as curettage and trachelorrhaphy, which necessitate pulling the uterus into the vaginal plane.

Palliative therapy resolves itself into the application of a **pessary** in cases of replaceable retrodisplacement, and the treatment of coexisting parametritis and adnexal disease when the uterus is thereby immobilized.

There are 4 types of pessary well adapted to the treatment of retroversion under slightly different conditions: The Hodge; the Albert Smith, the Thomas, and the Findley, of which the Smith is the most popular. The purpose of a pessary is not to correct a displacement but to maintain proper uterine poise after the uterus has been replaced. Certain prerequisites are essential: The bladder should be emptied by catheter, the mobile uterus must be replaced bimanually; there must be no associated prolapse or extensive cystocele, and before an appliance is selected for an individual patient the size and configuration of the vagina should be estimated. The length is determined by inserting the fingers high in the posterior fornix, just as though measuring the diagonal conjugate diameter of the pelvis. The approximate width is estimated by separating the finger tips at the midportion of the vagina It is thus easy to select a pessary of the size and shape that the patient needs

Laparotomy for the correction of displaced uterus is an elective and not an emergency procedure, and it should not be advised unless the hazards involved are minimal, all palliative measures have been exhausted and subsequent pelvic comfort can be anticipated

In reviewing his series of 429 cases, certain significant facts became apparent

1 Several operations by other surgeons for the cure of developmental defects were followed by recurrence.

2. Endowment with a congenital malposition does not condemn a patient to sterility.

- 3 After delivery the uterus may involute in normal position, even though previously congenitally retrodisplaced.
- 4. Symptomless acquired retroversions were discovered in patients presenting themselves with conditions such as Bartholin cyst, prunitis vulvae, trichomonas infections, cervical polyp, sterility, urinary complaints, colitis and breast tumor. They were commoner in postmenopausal women
- 5 Successful palliative treatment embraced careful preliminary differential diagnosis as well as the correct therapy for hormonal imbalance endocervicitis, parametritis and adnexal disease. In some instances a pessary was used after a fixed uterus became mobilized

In a series of 3400 consecutive office patients, a retrodisplacement was found 429 times, an incidence of 125 per cent; 142 of these were subjected to operation

No single surgical procedure is universally applicable. An operation which fails to afford symptomatic relief is a failure.

Submucous Myoma

Diagnosis—The indications for the use of x-rays and radio-opaque media and CO₂ for the demonstration of submucous myoma are given by I C Rubin³⁹ as follows

- 1 When it is important to avoid a laparotomy for fibroids as in the case of obese individuals and in systemic disease, in which circumstances x-ray and radium therapy is usually preferred. If a submucous myoma is positively known to be present, surgical removal is indicated despite the increased risk to the otherwise handicapped patient.
- 2 When considering myomectomy in younger individuals who are sterile and desire children, or when menstruation is to be conserved, the knowledge of the presence of a submucous myoma will enable the surgeon to deal adequately with the condition, adopting suitable vag-

inal or laparotomy technic, or a combination of the 2.

Hippuran has so far been used. It is available in crystalline powder and can be made up into 100 per cent solution, in which state it can be kept at a moderately warm temperature. When cooled, it crystallizes, requiring heating before the injection. In this saturation it remains a clear solution for a half hour or somewhat longer

The hippuran is introduced into the uterine cavity by means of a 20 cc syringe and uterine cannula, both of which are kept warm. An x-ray exposure is made at the point when the uterine cavity is filled. As a rule, from 5 to 10 or 15 cc. are needed in fibromyomatous uteri under pressures varying between 40 mm. Hg and 150 mm. Hg

After the x-ray exposure is made, the hippuran is withdrawn into the syringe and the cannula is removed. It is well to allow 2 or 3 minutes for the uterus to empty itself. The solution is aspirated and whatever amount remains is expelled. Another syringe filled with 20 cc. CO_2 is now attached to a clean cannula, 1 or 2 cc being discharged into sterile fluid in order to displace the air contained in the uterine cannula. The cannula is introduced into the uterine cavity and the CO2 is injected until a sense of resistance is reached which is similar to that experienced during the injection of hippuran. At this point an x-ray exposure is made

The presence of submucous myomas, Rubin shows, can be diagnosed roentgenologically by the intrauterine injection of hippuran followed by CO_2 . Neither by itself is adequate for this purpose. The hippuran when expelled from the uterine cavity, leaves a crystalline deposit on the uterine mucosa and the mucosa covering the submucous tumor. The injection of CO_2 serves as a transparent contrast to

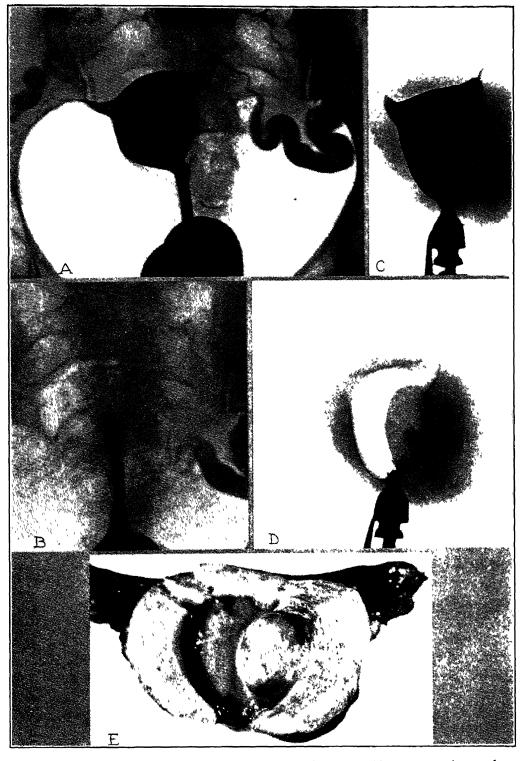


Fig 1—Case M M—A, clinical hysterogram with hippuran 100 per cent solution shows a dilated cavity without any definite indication of a submucous fibroid B, clinical hysteroaerogram with CO2 injected after hippuran shows the uterine cavity to be definitely encroached upon by a submucous myoma C, hysterogram of extirpated uterus with hippuran 100 per cent solution, no indication of a submucous fibroid D, hysteroaerogram of extirpated uterus with CO2 after hippuran shows the solitary submucous fibroid practically as it appears in E E, uterus cut open shows the submucous fibroid visualized in hysteroaerogram, D (Rubin Am J Obst and Gynec)

the densely opaque hippuran outline. Both media are innocuous, each being well tolerated by the organism. There are no irritation and no residue or foreign body reaction. In selected cases where recognition of submucous myoma is important from the viewpoint of the choice of therapy, this method appears to be serviceable.

VAGINA

Imperforate Hymen with Hematocolpos

Treatment—A review of 113 cases in the literature and a report of 5 additional cases is made by P Tompkins 40

Hematocolpos results from complete vaginal obstruction to menstrual flow Such obstruction during adolescence is usually caused by an imperforate hymen, but occasionally it is due to congenital retrohymenal atresia or to agglutination of the labia as a result of chronic infection and uncleanliness. Hematocolpos has also been reported in cases of double vagina when I outlet is occluded. In any case, blockage of menstrual flow produces first dilatation of the vagina, later dilatation of the cervix and uterus, and finally dilatation of 1 or both tubes. This condition does not lead to endometriosis

The dammed-up blood is thick, dark and "molasseslike" or "tarry". In addition to the 3 principal symptoms, amenorrhea, pelvic pain and disturbances referable to the bladder, there may be abdominal enlargement, a protruding mass at the vulva or pain on sitting

The suggested plan of treatment offered by Tompkins is as follows:

- 1 Meticulous preoperative preparation of the vulva and perineum
- 2 Complete excision of the hymen, not simple incision

- No vaginal examination at the time of operation.
- 4. After evacuation of the hematocolpos on the operating table a careful rectal examination to determine whether there is distention of the tubes. If there is evidence of hematosalpinx, laparotomy should be performed and the tubes should be incised and drained or, if necessary, removed.
- 5 A postoperative vulvar dressing of gauze soaked in *mercury bichloride* solution.
- 6 High Fowler position to promote drainage
- 7. Enough *morphine* to produce constipation for at least 4 days after operation
- 8 Careful cleansing of the perineum after every evacuation.
- 9. At least 1 week of rest in bed (in the Fowler position) after the temperature is normal
- 10 No tub bathing or swimming and no douching until 2 menstrual periods have occurred
- 11. No vaginal examination until 2 menstrual periods have occurred. This examination should be made with sterile precautions

Evaluation of Human Vaginal Smear in Relationship to Histology of Vaginal Mucosa

S II Geist and U J Salmon⁴¹ report their results with vaginal biopsies taken from the left forms of the vagina from a group of 60 women with varying degrees of estrogen deficiency (menopause, surgical and x-ray castration) The degree of regression was compared with vaginal smears (prepared by the fuchsin method) before and after treatment with an active estrogen. The vaginal smears and vagmal mucosa were classified into groups, representing various degrees of estrogen deficiency. The vaginal smears according to this classification were found to correspond with graded degrees of atrophy of the vaginal mucosa After treatment with estradiol, the changes in the vaginal smear reflected clearly the regenerative changes in the mucosa. Atrophy of the vaginal mucosa was found in many cases not to be uniform in degree,

GYNECOLOGY

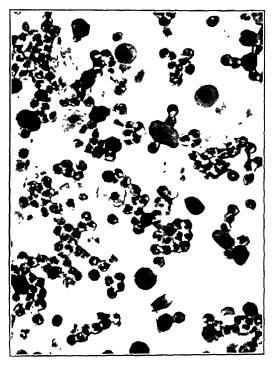


Fig 2—Reaction I Advanced estrogen deficiency Vaginal smear taken from patient B L, aged 54, 9 years after menopause. The smear contains the typical "atrophy cells," leukocytes, and a few erythrocytes. (Geist and Salmon. Am. J. Obst. & Gynec.)

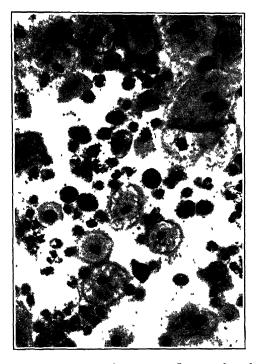


Fig 3—Reaction II Moderate estrogen deficiency Smear taken from patient S B, aged 48, 4 years after bilateral ovariectomy. Note presence of moderate-sized epithelial cells as well as "atrophy cells," leukocytes, and erythrocytes (Geist and Salmon Am J Obst & Gynec)



Fig. 4—Reaction III. Smear taken from patient J W, aged 43, 10 months after spontaneous menopause. The epithelial cells are larger than in the Reaction II smear (Fig. 3). They vary in shape, are irregular in outline and have a tendency to form in clumps. (Gerst and Salmon. Am J Obst. & Gynec.)



Fig 5—Reaction IV The cells are large and flat, the edges clean cut, nuclei pyknotic No "atrophy cells" are piesent. Smear taken on the eighteenth day of the cycle from young woman, aged 23, with a normal, regular menstrual cycle (Geist and Salmon Am. J. Obst. & Gynec.)

being more marked in some areas than in others. The regenerative process resulting from estrogen administration likewise does not manifest itself uniformly. Vaginal smears prepared by the fuchsin method were found to reflect the degree of regression as well as of regeneration of the vaginal mucosa in women.

The fuchsin vaginal smear method is recommended by these authors, there-

because the administration of antimony compounds caused loss of motility and finally disappearance of these organisms. Certainly, such organisms can be demonstrated in the superficial secretion from the surface of the lesions, both by dark field examination and by stained smears, but are not found after the surface detritus and pus has been completely removed or in material obtained from

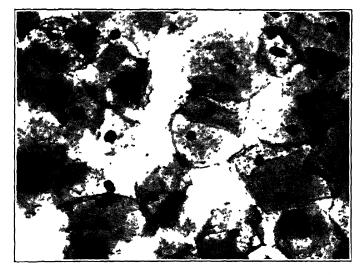


Fig. 6—Vaginal smear taken from patient B L, after 120,000 R U estradiol by mouth Compare with pretreatment smear (Fig. 2) (Geist and Salmon Am. J. Obst. & Gynec)

fore, as a simple, reliable procedure for determining the presence of normal ovarian activity or estrogen deficiency, as well as an indicator of the efficacy of administered estrogens in cases of estrogen deficiency

VULVA

Granuloma Inguinale

Thirty-five years ago Donovan reported that certain encapsulated organisms were the cause of granuloma inguinale. In September, 1937, Butts stated that spirochetes and rapidly motile bacilli, found in 8 cases of granuloma inguinale, were the cause of this disease,

the base of the lesion Morphologically these spirochetes are of the refringens type and the motile bacteria are fusiform bacilli. On the other hand, the encapsulated and nonencapsulated organisms known as the Donovan bodies are to be found in all undoubted clinical cases of granuloma inguinale and, if material is obtained from the base of the lesion, only these bodies are found

Granuloma inguinale was experimentally reproduced by R. B. Greenblatt, R. B. Dienst, E. R. Pund, and R. Torpin⁴² in 3 human beings but failed to develop in laboratory animals in spite of repeated attempts. When the disease was reproduced, the course was comparable in every way to that seen in

spontaneous cases. Donovan bodies were recovered to the exclusion of other organisms from the pseudobuboes that developed in each of the 3 patients. The incubation period could not be determined; however, the classic of the disease was full blown in about 50 days. This is the first instance in which granuloma inguinale was experimentally produced in a human being by the use of an exudate which contained only the Donovan body and no other demonstrable organisms.

The pseudobubo that so frequently follows a primary focus on the external genitalia is not an adenitis per se but a subcutaneous granuloma The histopathologic study of regional and underlying lymph nodes revealed but a moderate endothelial hyperplasia However, in 2 patients, 1 of whom also had extragenital involvement, Donovan bodies were demonstrated in the underlying cervical and inguinal lymph nodes, and in the other in 1 regional inguinal node Such observations prove that the Donovan body can and does travel by way of the lymphatics. The hypothesis is presented that Donovan bodies may reach the lymph nodes, where temporary though mild focal reactions with perilymphadenitis occur. During this process Donovan bodies may reach the papillae and corium of the overlying skin and set up a subcutaneous granuloma. Here the process may be subacute, resulting in a subcutaneous abscess, or may be chronic and a massive granulomatous tissue bulges the overlying epidermis. Hence the pseudobubo, for prior to rupture and the burgeoning of the typical raised granulations, it simulates the bubo of the other venereal disease.

The nature of the Donovan body remains an enigma. The method of reproduction in mononuclear endothelial cells and the growth requirements of the or-

ganism as well as the clinical behavior of the disease lead the authors to assume that the Donovan body is a sporozoan

Pruritus of the Anus and Vulva

Howard Hailey and Hugh Hailey⁴³ state that the majority of cases of true pruritus of the anus and vulva are due to eczema, the causes of which are essentially the same as those causing eczema in other anatomic localities. The patient's heredity makes a suitable soil for the development of the eczema, as it does for the development of asthma, hay fever, urticaria and migraine in hypersensitive persons. Pruritus of the anus and vulva, in fact, is eczema of those regions and as such is a manifestation of hypersensitiveness in the skin. The direct causes which bring on the attacks may be chemical substances, including some drugs and dyes, clothing, including wool; rubber and some synthetic fabrics, hemorrhoids, diet, heat, atmospheric condition or perspiration and friction

These investigators believe that, if it were always possible to obtain a reliable history, almost every case would give a history of hypersensitiveness in the family In their series of 105 cases, more than 60 per cent gave such a history of manifestations of hypersensitiveness. Benefit in the way of treatment was offered by the roentgen ray. They obtained climcal cures lasting from months to years in 80 per cent of their cases and iniprovement in an additional 15 per cent. One should insist, however, on having an accurate record of any previous roentgen treatment in order to avoid possible unfortunate sequelae.

Vulvovaginitis

Treatment — C. Mazer and F R. Schechter⁴⁴ report their study of a group of 118 children ranging in age from 18 months to 11 years, admitted to the

wards of the Philadelphia General Hospital for the treatment of gonococcic vulvovaginitis. The diagnosis in each case was based on clinical symptoms and on the presence of gram-negative intracellular diplococci, structurally characteristic of the gonococcus in the vaginal Since the children were hossmear. pitalized during the entire period of treatment, there was an excellent opportunity to observe the response to the administration of estrogen. About onethird of the children were in the acute stage of the illness at the time of ad-The duration of the disease in mission the others ranged from 2 months to 2 There was no appreciable difference in the response of the respective groups to treatment with estrogen.

Eighty-one of the 118 children were treated by means of hypodermic injections of estradiol benzoate (progynon-B); 34 received the same product as vaginal suppositories, and the remaining 3 were given estradiol (progynon-DH) orally.

1. Hypodermic Administration of Estrogen—Sixty-one of the 81 children hypodermically treated received from 1000 to 1500 rat units and 7 were given 500 rat units every other day for a period of from 4 to 6 weeks.

The first of 4 consecutive vaginal smears was obtained after 2 weeks of treatment in 46 cases, in the fourth week of treatment in 14, and during the fifth week in 18. The vaginal discharge was then scanty thick and snow white, revealing a mass of non-nucleated epithelial cells and gram-negative bacilli on smears. In the remaining 3 the vaginal smears were persistently positive, possibly because of inadequate vaginal drainage of accumulated débris, which in itself may have been a source of irritation. In order to evaluate treatment with estrogen accurately, no attempt was made to

dilate the introitus or to irrigate the vagina for the purpose of removing the plugs of desquamated epithelial cells.

Sixty-one of the 78 children successfully treated with estrogen hypodermically were followed for a period of from 3 to 23 months, with an average of 10 months for the entire group. There were only 6 (10 per cent) recurrences in the 61 followed-up patients who had received treatment for 8 weeks and 2 in the 8 who had received treatment for a period of only from 4 to 6 weeks. Notwithstanding the fact that the comparison is made on too few patients, it is nevertheless significant that the incidence of recurrences in the group of 8 followedup patients who had received the relatively short treatment was 3 times greater than in the group treated for the full period of 8 weeks. Equally significant is the fact that recurrences with shorter treatment were not only more numerous but appeared much earlier (from 4 to 6 weeks after treatment), suggesting that incomplete cure was the cause of the trouble.

Side effects other than growth of pubic hair occurred more frequently and were more intense with adequate hypodermic treatment than with vaginal suppositories. Twenty-one of the 81 children (26 per cent) showed enlargement of the breasts, which persisted for about a month after withdrawal of the treatment; 7 (85 per cent) had a scanty growth of pubic hair, which eventually disappeared, and 8 (10 per cent) had a single episode of uterine bleeding either during treatment or later.

2. Treatment With Vaginal Suppositories of Estrogen — Thirty-four children were treated with vaginal suppositories, each containing 200 rat units of estradiol benzoate (progynon-B), inserted nightly on retiring for a period of 8 weeks.

A clinical cure and 4 consecutive negative vaginal smears were obtained during the fourth week of treatment in 33 of the 34 children The remaining patient failed to respond to vaginal as well as to subsequent hypodermic treatment with 1500 rat units given every other day for a period of 8 additional weeks.

The side effects with vaginal suppositories of estrogen were less pronounced than with hypodermic treatment. In 8 of the 34 patients there was a moderate enlargement of the breasts; in 6 there was a semblance of pubic hair growth and in 1 a single episode of menstruation. This child was, moreover, 11 years old and might have menstruated irrespective of the treatment

Twenty-six of the 33 children treated with vaginal suppositories and discharged as cured were followed for a period of from 3 to 13 months, averaging 7 months There were no recurrences

Oral Treatment—In 3 patients, oral administration of 1500 rat units daily of estradiol (progynon-DH) for a period of 8 weeks failed to accomplish a cure. They were subsequently treated by other methods. In the human being as well as in the experimental animal the minimum effective oral dose of estrogen must be 5 times greater than the hypodermic dose

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ABORTION

Significance of Endocrine Assays in Threatened and Habitual Abortion—J. S. L. Browne, J. S. Henry and E. H. Venning¹ report their study of the excretion of prolan, estrogens, and sodium pregnandiol glucuronidate in the urine of 35 cases of threatened or habitual abortion

Sodium pregnandiol glucuronidate is an excretion product of corpus luteum hormone and is believed to reflect the amount of progesterone being formed in the corpus luteum or elsewhere. This compound is absent from the urine during the follicular phase and first appears about 24 to 36 hours after ovulation. In most normal individuals, the excretion lasts for 10 to 12 days and the total amount excreted is between 45 and 55 mg expressed as pregnandiol Ordinarily, the excretion stops 1 to 3 days before the onset of bleeding, but in a few cases the excretion continues up to the time of bleeding

In early pregnancy, the level of excretion is the same as the maximum reached during the normal menstrual cycle, that is, from 5 to 10 mg per 24 hours The time at which the excretion of pregnandiol begins to rise from this level varies considerably in presumably normal cases, but it is most often between the seventieth and nmetieth days after the beginning of the last menstrual period. The amount excreted rises usually parallel to the rise of total estrogens and reaches a maximum in the ninth month The maximum is very variable, usually between 60 and 105 mg. per 24 hours, in some cases somewhat lower, and the compound disappears abruptly within 24 hours of delivery.

It is probable that the chorion begins to secrete this substance almost immediately on implantation. If the corpus luteum secretes progesterone for only 7 days after ovulation instead of 10 or 12, then by the time the ovum is ready to implant the corpus luteum will have ceased to function and implantation will not take place, since degeneration of the endometrium or even menstruation has begun. Such a short corpus luteum phase has been observed in some patients with sterility in whom no other cause for infertility has been detected. The rapid rise in production of prolan in early pregnancy may be necessary for increased stimulation of the corpus luteum to maintain it as it grows older

In normal pregnancy, pregnandiol excretion may begin to rise from the level obtained after implantation as early as the seventieth day or perhaps a little earlier, but in other cases the rise fails to occur until the hundredth day without any abnormal symptoms manifesting This rise is interpreted as themselves due to the beginning of secretion of progesterone by the placenta The rate of secretion gradually increases after this time up to term. Progesterone ceases to be formed when the placenta separates, and its excretion product disappears from the urine shortly after this. The chorion is the source of prolan from conception to term. In the first part of pregnancy, estrogens and progesterone are formed in the ovary. At a varying time, but usually from the seventieth to ninetieth day, the placenta begins to secrete these substances In most cases the corpus luteum ceases to function shortly after this The placenta continues to form these substances in gradually increasing amounts

until term. There is a transfer of function from 1 site of formation of progesterone and estrogens to another occurring usually in the third month.

The first of these cases analyzed were spontaneously occurring abortions in the early part of pregnancy. The assay findings probably depend upon the time in pregnancy at which the gestation ceased to develop and the length of time which had elapsed before assays were done as well as upon the degree of degeneration which had occurred in the placenta. It may be said that the placenta (chorion) begins to form prolan before it begins to form estrogens and progesterone. If the gestation ceases to develop before the placenta has begun to form these substances to any extent then apparently it seems not to go on to develop that function, or if it does, loses it before the time of assay in these cases, even though it remains in contact with the maternal circulation and continues to secrete prolan

In the second group analyzed are included the cases of threatened abortion. It is in these cases that the difficulty of determining the effect of various forms of therapy arises. In this and the next group are included cases which fall into the class of habitual abortion.

The authors believe that the time at which a deficiency of corpus luteum hormone is most likely to occur is therefore in the transion period between the ovarian and placental phases (late second and third months); this is the critical period of pregnancy.

The cause of many abortions is a faulty gestation from the first, the chorion partakes in this abnormality and produces an amount of gonadotrophic substance inadequate to prolong the corpus luteum beyond a certain point. In other patients where the gestation is less abnormal, the function of the corpus luteum may be

prolonged for the usual time and the embryo develop normally, but the placenta may be slow in taking over. In either case abortion follows. Patients in whom either of these conditions repeatedly occurs habitually abort.

With regard to therapeutic use of progesterone, pregnancy urine extracts. vitamin E, etc., in the treatment of threatened and habitual abortion, numerous claims for good results have been made. The present study shows how difficult it is to evaluate the results of such therapy. The use of gonadotrophic extracts where such large amounts are present as in early pregnancy seems likely to have little effect. In those patients where the prolan excretion is consistently low, in most cases the gestation is already degenerate. In those patients with abortion in whom the gestation is degenerate before the onset of symptoms, progesterone is obviously abnormal from the first, and even if therapy is started before symptoms appear, the result will be unsatisfactory. The patients in whom the embryo and placenta develop up to a certain period, but the placenta takes over the function of progesterone formation late or the corpus luteum degenerates early, offer theoretically the most hopeful outlook for progesterone therapy, since in many, if the critical period can be tided over, the placental function begins and further therapy is unnecessary. It is possible that the determination of prolan excretion in early pregnancy may enable one to distinguish patients in whom the gestation is already degenerate from those in whom therapy might be of benefit However, as shown in this investigation, a single determination is of no value, since patients showing temporary low prolan values in early pregnancy, do carry through to term.

The question of dosage is difficult to determine. From the pregnandiol assays, it seems obvious that the amount of progesterone produced by the corpus luteum up to the seventieth or eightieth day is 5 to 10 mg. per day, and that the placenta produces a gradually increasing amount as pregnancy advances.

Therapeutic doses of less than 5 mg. are unlikely to have much effect. This dose should be given daily, or every other day, and may be increased in the presence of persisting symptoms. most cases either of the threatened or habitual type, therapy should be concentrated during the period of transfer of the function of formation of progesterone from ovary to placenta, since it is at this time that abortion is most likely to occur. If pregnandiol assays are available, a definite rise in pregnandiol excretion may be taken as an index that further therapy is probably unnecessary. The danger of wasting treatment on an already dead fetus, and the uselessness of treating a patient after her own placenta has begun to form normal amounts of progesterone, should always be borne in mind

Hypothyroidism in the Causation of Abortion—E. L. King and J S. Herring² attempt to evaluate hypothyroidism as a cause of abortion. Their report represents a study of the basal metabolic rate of 150 pregnant women, all private patients. The readings were taken in the early months of pregnancy except in 2 cases, in which it was first taken after miscarriage had occurred. The association of abortion with rather marked hypothyroidism had previously been noted in several instances.

Of these 150 women, 17 were found to be hyperthyroid (basal metabolic rate plus 10 or over), 72 had normal readings and 61 (or 40.6 per cent) were hypothyroid Of the 17 in the first

group, 5 were multiparas; 3 of these had aborted in a previous pregnancy Of the 72 women with normal rates, 10 were multiparas with 4 previous miscarriages. There was only 1 abortion in this group; 8 threatened abortions were averted. However, the patients with rates between minus 6 and minus 9 were given small doses of *thyroid extract* prophylactically, especially if they had aborted in previous pregnancies. The authors feel that this was a factor in reducing the number of abortions.

The authors conclude that hypothyroidism of mild or moderate degree is a fairly common complication of pregnancy. The severer types, particularly when associated with the same condition in the husband, will be found to be productive of sterility.

ANALGESIA

Effects of Obstetric Analgesia on the Newborn Infant — Eight hundred consecutive babies born of mothers delivered by the vaginal route in private practice were selected for this study by J Kotz and M. S Kaufman.³ In 500 instances the mother received paraldehyde either alone or in combination with some other drug, in 100 instances she was treated by the McCormick modification of the Gwathmey technic and in 100 she received pentobarbital sodium and scopolamine. The babies of 100 mothers who received no analgesia were used as controls.

In these groups the following factors were studied: (1) The mortality rate, (2) the initial loss of weight; (3) the rate of gain for the first 10 days of life, (4) the temperature curve for the first 10 days of life, and (5) the pulse and respiration curve for the first 10 days of life. Also due consideration was given to the duration of labor, the type of deliv-

ery, the dosage of the analgesia used and its effect on the subsequent clinical course of the infants after birth

One hundred additional cases were selected for a more detailed study. In 50 the mother received paraldehyde analgesia. In each of these cases the infant was matched with another child, born on the same day and of approximately the same birth weight but whose mother received no analgesia. The 2 babies were fed identical formulas and the environmental conditions were the same. In these cases the temperature, pulse and respiratory rates were recorded every 4 hours and the weight was checked twice a day for the first 3 days of life.

The time interval between delivery and the initial respiration was checked with a stop watch on 100 paraldehyde babies and 100 control babies

Dosage of Analgesia—The average dosage of paraldehyde was 17.5 drams (66 cc) given with an average of $^{11}/_{60}$ grain (0.012 Gm) of morphine sulfate. The usual initial dose was from 6 to 8 drams (23 to 31 cc) of paraldehyde by rectum and $^{1}/_{6}$ or $^{1}/_{4}$ grain (0.011 or 0.016 Gm) of morphine hypodermically, the paraldehyde being repeated in 3 or 4 dram (12 or 15.5 cc) doses as often as necessary

The largest total dose given was 38 drams (1425 ec) of paraldehyde and 1/4 grain of morphine. It is apparent and we wish to emphasize the fact that in this series of cases large doses of analgesia were used. If analgesia has an effect on the child, such effects would certainly be demonstrable in this group

In the group of mothers treated by the McCormick technic, the average amount given was 1 53 doses of the mixture and 4 99 grains (0 32 Gm) of pentobarbital sodium.

In the group receiving pentobarbital sodium and scopolamine the average

total dose was 678 grains (044 Gm.) of pentobarbital sodium and ½00 grain (0.0003 Gm.) of scopolamine.

The investigators concluded that obstetric analgesia, properly administered, does not increase the infant mortality or morbidity rates above those which occur in a series of infants whose mothers were delivered without analgesia

Etiologic Factors in Neonatal Asphyxia—In contrast to the above is a series of 5000 consecutive deliveries at the Woman's Hospital in Detroit analyzed by W. C C. Cole, D. C Kımball and L E. Daniels4 with a view of determining the relative importance of the various factors which contribute to the production of asphyxia in the newborn The maturity of the infant, the age, parity and health of the mother, the duration of the various stages of labor, the type of delivery and the use of sedatives and anesthetics all were found to exert important influences on the incidence of asphysia. They noted that these factors frequently operate in combination. These investigators conclude that the important single factor in the etiology of neonatal asphyxia is prematurity. The next most important factor is the trauma of labor, whether it is the normal forces of normal labor or whether it is accentuated by dystocia and operative delivery. Sedatives in any amount definitely increase the incidence of asphyxia in the baby in direct proportion to the amounts given General anesthesia in any amount defiintely increases the incidence of asphyxia in the baby in direct proportion to the duration of the anesthesia

Cyclopropane in Obstetrics

The effect of obstetrical anesthesia upon the oxygenation of maternal and fetal blood, with particular reference to cyclopropane was studied by C. A Smith.⁵ Determinations were made of

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the oxygen content of arterial and venous blood from women during labor. Similar determinations were made upon the arterial and venous bloods of 3 groups of mothers and their infants at the moment of birth. These 3 groups represented routine deliveries under ether, under nitrous oxide-oxygen, and under cyclopropane anesthesia. In the second and third of these groups, the amounts of nitrous oxide and of cyclopropane were also quantitatively determined in the maternal and fetal bloods An attempt was made to correlate the degree of oxygenation of maternal and fetal blood with the type of anesthetic used, and to discover the relationship between fetal anoxemia and the presence or absence of apnea in the newborn infant. The following observations seem significant:

- 1. Oxygenation of maternal blood during labor but before delivery and anesthesia was comparable to that observed by other authors for maternal blood at delivery without anesthesia. The arternal blood during labor showed a slight anoxemia.
- 2 Specimens of fetal blood at the moment of birth showed wide variations in oxygen content, presumably because of anatomical and other uncontrollable circumstances. As a rule, the fetal blood at birth, even on the arterial side, was considerably deficient in oxygen
- 3 In general, ether anesthesia produced a definite elevation of the maternal oxygen capacity, and of the oxygenation of maternal venous blood. Under this anesthesia the fetal oxygenation appeared to be satisfactory.
- 4. Nitrous oxide, administered with at least 20 per cent oxygen, produced a definite maternal and fetal anoxemia.
- 5 Under cyclopropane, the maternal blood showed a pronounced elevation of oxygenation in both the arterial and venous specimens
- 6 Pronounced anoxemia in the fetal blood at birth was not constantly accompanied by apnea of the newly born infant, except in babies delivered under nitrous oxide-oxygen. Fetal anoxemia is probably one of several factors which may operate to produce apnea A surprising degree of fetal anoxemia may be associated with a normal onset of respiration.

- 7. Cyclopropane was present in the fetal blood in almost as high concentration as in the maternal blood. However, only about half as much nitrous oxide was found in the fetal as in the maternal blood.
- 8. Judged by biochemical data, cyclopropane as an obstetrical anesthetic would appear to be perhaps less safe for the infant than the clinical appearance of the mother would indicate.

LABOR

Cause—A thorough consideration of the cause of the onset of labor is offered by D. N. Danforth and A. C. Ivy.⁶ The following subjects are discussed:

- 1 The rôle of nervous mechanisms.
- 2 The present concept of the rôle of the estrogenic and progestational hormones
 - 3 The rôle of the placenta
- 4 The effect of mineral ions upon the uterus.
- 5. The effect of the estrogenic and progestational hormones upon mineral metabolism
- 6. Alterations in blood volume, blood proteins, and acid-base balance in pregnancy

The minor or negligible influence of nervous mechanisms as primary causative factors is pointed out. Although the precise mechanism by which the hormones act is unknown, it has been demonstrated that in all likelihood gestation is maintained by progestin, and labor precipitated by estrin. The essential rôle of the placenta in regulating the proper concentrations of these hormones is stressed.

Calcium has been shown to be essential for uterine contraction. The similarity of the uterine response to progestin and to calcium deprivation, and of the response to estrin and calcium in excess is emphasized. The acid-base balance of the body is an important factor in the regulation of the availability of calcium, a relative alkali deficit favoring its activity.

There is evidence in support of the contention that the plasma alkalı deficit

and increased blood volume of pregnancy are dependent upon the interaction of the estrogenic and progestational hormones, and are brought about through the ability of these autacoids to regulate the metabolism of sodium, or fixed base. In spite of the fact that both groups of hormones produce sodium retention, only one, progesterone, is capable of acting as a cortical substitute. This seems to be direct evidence of the fact that the retention due to estrin influence is different from that due to progestin. When one progresses further than this, unstable ground is reached However, it is not unlikely that through alterations in the metabolism of fixed base, which have been shown to occur as the result of the influence of these substances, the utilizable fractions of calcium, and other essential ions might be altered secondarily and the motility response of the uterus so Such a hypothesis, though obviously incomplete, might aid in the explanation of the delayed response of the myometrium to injections of estrin and progestin, might point to certain therapeutic measures which are more direct than the use of glandular extract, and, further, might indicate a fundamental approach to the problem of the regulation of uterine contractility Proof of these postulations must await a satisfactory method for the estimation of ionic calcium

The precipitation of labor at term is not due to any 1 factor, but rather results from a combination of many. Among the factors which would contribute to so "priming" the uterus are. (a) The increasing estrin concentration in the face of apparently regressing progestin levels; (b) the probable increase in active calcium, and (c) increasing distention, which invariably produces gradually increasing contractions in any hollow viscus

Cesarean Section

Cerebral Defects in Children Delivered by Cesarean Section-T. Brander,7 in reviewing the literature, found 72 cases of intracranial lesions verified post mortem in children who had been delivered by abdominal cesarean section (cases of vaginal cesarean section excluded). In some of these cases, a tearing of the tentorium was discovered There are also numerous observations on symptoms of intracranial birth injuries, such as defective intelligence, epileptiform convulsions and spastic pareses The author describes the clinical histories of 3 children with mental defects who had been delivered by cesarean operation. He admits that in the cases of severe cerebral defects the hereditary conditions are not always sufficiently clear Morover, the reports in which the diagnosis of intracranial lesions in children delivered by cesarean operation cannot be doubted contain nothing about the obstetric complications that led to the cesarean operation. In this connection, the author points out that the fetus may have been injured by attempted forceps extraction before the cesarean operation was resorted to. The same applies to cases in which prolonged labor pains, perhaps in connection with Walcher's position, preceded the operation. If at this time the head of the child was tightly wedged into the pelvic inlet it may be injured not only before but also during the cesarean operation

Intracranial birth injuries in connection with the cesarean operation occur more frequently in vaginal than in abdominal cesarean section, and of the abdominal methods the corporal involves less dangers for the fetus than does the cervical method. Moreover, the extraction by the foot seems to be more dangerous than freeing the head first, and

instrumental development of the head is, of course, more harmful than is its manual extraction. In cases in which the fetus is large, too short incisions may increase the danger of an intracranial lesion Complications may arise if the surgical incision injuries the placenta. The danger of intracranial hemorrhages in the course of cesarean operations is greater in premature deliveries, in the hemorrhagic diathesis and in pregnancy toxicoses. Asphyxia supposedly may cause intracranial hemorrhages; on the other hand, it is probable that intracranial injury may become manifest in asphyxia That methods of resuscitation may cause intracranial hemorrhages in children delivered by cesarean operation has likewise been observed.

Bacteriology of the Uterus at Cesarean Section—An analysis by T. K. Brown⁸ of 144 uterine cultures taken at cesarean section is presented in order to demonstrate the apparent value of antiseptic vaginal instillations in the preparation of the patient for operation. Cultures were obtained from 52 per cent of the patients operated upon during a period of 8 years at the St Louis Maternity Hospital. A very practical finding is that when a case has received the benefit of antiseptic vaginal instillations before operation, the time of operation may be safely postponed much longer than has been formerly recommended

One per cent neutral acriflavine in glycerin is instilled into the vagina because of the rather specific affinity of acriflavine for cocci. Eight cubic centimeters of the solution are instilled into the vagina upon admission of the patient and every 4 hours. In numerous cases, the degree of penetration of this dye substance has been observed to extend 4 inches above the external os.

In this series only 4 1 per cent positive uterine cultures were obtained with the

routine use of acriflavine instillations. With the use of antiseptic instillations, the period of time in labor may be greatly prolonged with negative cultures being obtained as late as 107½ hours after the onset of labor.

The author concludes that antiseptic vaginal instillations offer a means of preparation of a patient for cesarean section which will (1) largely eliminate one of the most important causes of mortality, infection; (2) reduce the incidence of positive uterine cultures obtained; (3) make it relatively safe to postpone operation until a much later hour in labor; and (4) lower the indication for the more radical operative procedures Of course intrapartum infection may occur and this can only be prevented by the earlier prophylactic use of the instillations

Complications of Labor

Hemorrhage—Insufficiencies of Anterior Hypophysis Following Hemorrhages - G Effkemann and F. Muller-Jager⁹ point out that it has been reported that ischemic necroses of the anterior lobe of the hypophysis develop frequently after severe partum and postpartum hemorrhages. They also mention observations by Erdheim and Stumme on the gravidic hyperplasia of the hypophysis and then cite numerous clinical pictures indicating a hypophyseal disorder which are observed following childbirth Since in the literature it is stated repeatedly that such disorders are the result of severe postpartum hemorrhages, the authors decided to make follow-up examinations on women in whom childbirth had been complicated by severe hemorrhages. They were able to reexamine 86 women who had given birth during the years 1928 to 1935 found that genital atrophy with hypomenorrhea, sterility and adiposity were

comparatively frequent in these women in later life. It is probable that these manifestations are connected with the postpartum hemorrhages. Moreover, hygalactia, emaciation and menstrual anomalies also showed a more than normal frequency in this material.

The authors show that there are many factors which indicate that these symptoms are not caused by the postpartum hemorrhages but that these hemorrhages or atony are more frequent in the women with the endocrine predisposition for the aforementioned symptoms. They also reject the theory that the postpartum hemorrhages contribute to the pathogenesis of endocrine disturbances that are due to impairments in the hypophysealdience-phalic system. They think that women with a latent predisposition to such endocrine disorders are also predisposed to postpartum hemorrhages.

Obstetric Shock—Pathology—In a study of the pathologic anatomy of obstetric shock, H L Sheehan¹⁰ reviewed all the fatal cases of obstetric shock seen in the Glasgow Maternity Hospital during the previous $5\frac{1}{2}$ years. The criterion of obstetric shock that was adopted is wider than that in common clinical use, that is, if the patient with the clinical appearance of shock died during labor or within 24 hours after delivery, whether or not any explanation for the shock had been recognized before death. The cases finally selected were grouped according to the apparent etiologic factors. Dystocia, 29 cases; uncomplicated cesarean section, 4 cases, and complicating disease, 8 cases The cause of dystocia was simple disproportion, occipitoposterior presentation or, more rarely, hydrocephalus or oblique intrauterine position.

The second group, in which ruptured uterus was regarded as the cause of death, was closely related to the previous group Seven of these patients had

dystocia requiring intrauterine manipulations; the other 6 patients had spontaneous ruptures. The retained placenta group could be divided into 6 patients who died between 2 and 3 hours after delivery and 16 patients, of whom 11 died between 4 and 8 hours after delivery and the other 5 between 8 and 24 hours after delivery. The 21 cases in the uteroplacental apoplexy group were so called as representing mixed or concealed accidental hemorrhage with retroplacental clot Although these cases are usually classified under the heading "hemorrhage," the usual cause of death is shock. Of the 8 cases due to complicating disease, death occurred in 1 before delivery and in the others within 8 hours after delivery Four of the patients had definite evidence of previous hypertension, the others had lobar pneumonia, acute hemorrhagic pancreatitis, renal disease and influenza respectively

The principal characteristic demonstrable organic pathologic changes given by Sheehan consisted of the presence of subendocardial hemorrhages on the left of the interventricular septum, a uterine appearance dependent on the clinical condition, occasional hemorrhages into the ovaries, edema of the parametrium and pelvic tissues in some instances, acute dilatation of the stomach with air, commonly, and necrosis of the anterior lobe of the pituitary gland, if the patient who died of obstetric shock survived for a day or ore

Treatment — The treatment of obstetric shock is discussed by H. B. Matthews. 11 Prolonged labor produces muscle fatigue, which is shown by the gradual increase in pulse rate, slowing of uterine contractions, tendency of the tongue to become dry, intestinal distention, and usually some rise in temperature. The tired parturient patient is a poor operative risk. Furthermore, anes-

thesia upsets the balance between the constituents of the protein radical, which has already been disturbed by the pregnancy. In such cases a dose of *morphine* secures both physical and uterine rest, and an intravenous injection of from 100 to 200 cc of a 50 per cent *dextrose* solution will completely change the patient's appearance, as the pulse is slowed and both the systolic and pulse pressures are improved If fluid is needed, 75 Gm. of dextrose in 500 cc. of saline solution may be given from 3 to 5 cc. per minute.

Experience indicates that nitrous oxide anesthesia is less likely to precipitate shock than either ether or chloroform. The author ridicules the many who still attempt to secure slower, stronger pulse, and improved heart action by digitalization of patients who are shocked and Equally illogical is the atmoribund tempted treatment of shock with vasoconstrictor drugs, such as epinephrine Apparently, some have not sensed that in shock the arteries are not relaxed. but are markedly contracted. Not only is this agent useless; it has grave potentialities if given in excess of physiologic doses.

Evidence has been presented indicating that *adrenal cortical extract*, given by injection, aids in preventing shock

The use of *pitressin* has been suggested because of its effects in producing contraction of the capillaries

Morphine, in sufficient dosage, should be used in shock to relieve pain and allay restlessness. If bleeding is or has recently been present, it should be given to quiet the circulation. When marked cyanosis is present, some sedative other than morphine, for obvious reasons, is indicated.

Many writers have advocated the use of *caffeine*, and a few believe that *strychnine* is beneficial. It is uncertain whether

these suggestions are based on sound experience or on theory.

Various mechanical means for aiding the return of venous blood have been employed. The commonest of these is the Trendelenburg position. Other efforts advised consist in mechanical pressure applied to the limbs, such as an elastic binder, and sandbags to the abdomen. The suggestions recognize the factor of low venous pressure and they attempt to raise it by external pressure. The reasoning on which such suggestions are based is not entirely sound and does not take into account the fact that blood is not pooled in the veins but in the capillaries. Mechanical aids to combat the effects of low venous pressure are therefore of doubtful value.

Heat should be employed externally in every case of shock in an effort to improve peripheral circulation. No patient in shock can be successfully treated unless body temperature can be raised to within normal or nearly normal levels. Excessive heat, on the other hand, is contraindicated because it causes a loss of water and chlorides as the result of sweating.

The ideal method of treatment is to introduce some fluid into the blood stream that will cause an increase both in blood volume and in blood pressure. To accomplish this result, *blood* and its substitutes have been successfully employed. Whole blood is the ideal therapeutic agent for increasing the blood volume and blood pressure.

As an emergency measure, in the absence of blood or because of delay in obtaining the proper donor, it is usually necessary to use a substitute for blood in order to tide the patient over this critical waiting period. The results following the use of most of the substitutes have not been very encouraging. Isotonic saline solution has proved to be of little prac-

tical value. It will temporarily cause an increase in blood pressure, but, as the fluid injected passes into the tissue spaces, the blood pressure will in a very short time be as low as before and usually lower. Besides, with the injection of physiologic solution of sodium chloride there is a decrease in the total amount of plasma and at the same time a decrease in the percentage of protein in a unit volume of plasma. Therefore, isotonic saline solution will not cause an increase in the volume of blood in circulation because, with the diminished osmotic pressure, a decreased quantity of fluid is attracted back into the blood vessels from the tissue spaces. Weak solutions of dextrose have proved to be no more efficient. Solutions of acacia and of acacia with dextrose have their adherents. Acacia was added to saline solution in order to supply a colloid substance which would be retained by damaged endothelium. Later, acacia (6 per cent) was added to hypertonic dextrose solution and this method was successful in temporarily combating shock until transfusion could be given Other agents that have been used are 25 per cent gelatin, human ascitic fluid, and preserved human blood plasma.

Fearing the use of large quantities of fluid intravenously in "shocked cases," Matthews uses from $1\frac{2}{3}$ to $6\frac{2}{3}$ oz. (50 to 200 cc) of a 50 per cent solution of dextrose (usually 100 cc) with excellent results In cases in which acute shock was not the primary indication for the use of dextrose, 10 oz (300 cc.) of a 25 per cent solution in saline solution have been employed Hypodermoclysis of physiologic solution of sodium chloride is usually given immediately following the intravenous dextrose in sufficient quantity to supply the required fluid (water); i.e., from 2 to 5 quarts (2000 to 5000 cc) in 24 hours

PLACENTA

Use of Placental Blood for Transfusion

The pioneer work in the use of placental blood for transfusions on this continent was done by Drs. Goodall and Anderson, of Montreal, and their coworkers. Dr. Goodall not only brought to our attention the availability of placental blood for transfusions but also contributed a workable technic for the collection of the blood and its preservation. Dr Godall is an advocate of the "IPK" solution as proposed by the Moscow Institute of Hematology.

F E. Barton and T. M. Hearne¹² describe a modification of the technic of Goodall as practiced at the Massachusetts Memorial Hospital

Into a 300 cc. Erlenmeyer flask is placed 125 cc of 50 per dextrose solution To this is added, by weight, 100 cc. of freshly distilled water and the contents of an ampoule of citroseroid (25 The formula of citroseroid is sodium citrate, 5 Gm; sodium chloride, 7 (m; potassium chloride, 0.2 Gm; magnesium sulfate, 0.04 G.; and distilled water, 1000 cc. In Lindenbaum and Stroikova's original article, this formula is referred to as "IPK" A stazon rubber stopper is loosely placed in the neck of the flask. The flask is wrapped and autoclaved While the contents of the flask are cooling, the stopper is inserted in the neck of the flask without the wrapping being removed. This allows the exterior of the flask to remain sterile

The setup for the collection of the blood includes a flask containing the preservative, a pair of sterile mittens, a funnel, 3 small test tubes, a bottle of broth, a pipet, 2 Kelly clamps, and a pair of scissors. Following delivery, the cord is prepared with iodine, 2 clamps are applied and the cord is cut between the clamps.

The gloved hands are now covered with a pair of sterile mittens. The cord is again sharply cut proximal to the clamp. The end of the cord is pointed downward and the blood collected in the flask through a funnel. The cord may be milked to add to the yield.

As the flow diminishes, blood is collected in 2 small test tubes, 1 for a Wassermann test, and 1 for typing. The flask is slightly agitated and 10 cc. of the solution is obtained with a sterile pipet. One-half of the content is used to inoculate the broth for a check on contamination; the other half is placed in the third tube and stoppered with a cork stopper. The stoppered test tube containing a mixture of the blood and solution is attached to the flask with elastic bands. The flask is sealed airtight with a stopper and is not to be reopened until it is to be used for transfusion. The stoppered tube containing the mixture of blood and preservative is known as the pilot tube.

A tag is attached to the flask On this tag is recorded the name of the patient, the collection number, and the date and a space for type, Wassermann reaction and culture report. The flask is then placed on the lower shelf of the refrigerator and kept at a temperature of 38° F. (3.3° C). When the blood had been typed and the Wassermann reaction and culture reported negative, these data are placed on the tag and the flask is placed on the shelf above ready for use.

Placental blood may be collected on cesarean section. In these cases there is no chance of contamination. The only variation from the technic used in normal delivery is that the blood collected for the Wassermann test and typing is obtained after the placenta has been delivered.

When transfusion is contemplated, a flask of suitable type is chosen. A sample of the blood in the pilot tube is removed for direct typing. Usually 2 or 3 flasks are used for a single transfusion. These flasks are warmed in a bath and a continuous intravenous injection of physiologic of sodium chloride is started with an open Kelly bottle. A funnel is placed in the neck of the bottle with a gauze strainer and the contents of 1 flask are poured into the bottle.

The average yield of a flask is 100 cc. of blood. If a larger amount of blood is desired it may be added in a fractional manner, each flask added separately with a small amount of saline solution intervening between the contents of the flasks Reactions may follow if contents of 2 or more flasks are added together

The authors believe that the percentage of reactions during a transfusion need not be higher than a whole blood transfusion (1) if the blood is used before hemolysis sets in, (2) if the blood is used in a fractional manner, and (3) if the containers are kept airtight. They also believe that the blood is safe, economical, and efficacious.

The average quantity of placental blood that J. Howkins and H. F. Brewer¹³ collected from 50 consecutive women at term is small, 47 cc, which compares unfavorably with Goodall's and Grodberg's figures of 125 and 105 cc., respectively This small yield would necessitate the mixture of from 10 to 12 samples to supply the bulk of blood usually employed in an adult transfusion and it is questionable whether this extensive pooling of several bloods, although of the same group, is entirely devoid of the risk of the minor subgroup reactions of agglutination With regard to sterility, 22 per cent of the samples were contaminated with airborne or genital tract organisms (Bacillus subtilis, Bacillus coli, Bacillus procraneus and Streptococcus albus) after a reasonably aseptic technic

The authors can agree neither with Goodall in his assertion that culture of the collected blood is unnecessary nor with Grodberg in his statement that any stray organisms present are usually killed by the leukocytes—a statement which they have proved to be incorrect, in that their second culture always tallied with the first, and organisms if present on the seventh day of storage always survived

selected at random or because of clinical indications, were studied.

Technic—In general, no special preparation for cystography was necessary but an occasional patient needed an enema. Invariably the medium was instilled into the empty bladder and the catheter removed before exposure.

Media — Three contrast media were used: Sodium iodide in 25, 125, and

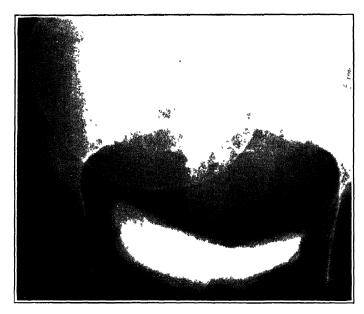


Fig. 1—Patient G. W. Anteroposterior cystogram diagnosed as indicative of placenta previa Central placenta previa found at time of cesarean section. (Prentiss & Tucker: Am. J. Obst. & Gynec.)

up to the time of subsequent culture. This source of blood for transfusion, however carefully perfected the technic of its collection, sterilization, and storage may become, is unlikely to rival seriously that available through the voluntary donor system.

Placenta Previa

Cystography in Diagnosis—R J Prentiss and W W Tucker¹⁴ discuss their method of precision for the roent-genologic diagnosis of placenta previa. One hundred and twenty patients, each in the last trimester of pregnancy and

25 0 per cent aqueous solutions, skiodan in 10 0 and 40 0 per cent aqueous solutions, and air. The weak solutions of sodium iodide gave poor delineation while the higher concentrations, although giving excellent vizualation, irritated the bladder. The 12 5 per cent solution, recommended by Ude and Urner, proved to be the most satisfactory.

Skiodan in 100 and 400 per cent solution outlined the bladder clearly but was costly. The liquid media in optimum quantities gave the relation of the bladder to the fetal skull, but failed to delineate clearly the space between these struc-

tures. More than 80 cc obscured the relations by causing the bladder and fetal skull shadows to overlap, thus entirely obscuring the space

On the other hand, air, as the contrast medium, not only outlined the bladder smoothly, but also pictured in sharp relief of the soft tissues intervening between the white shadow of the fetal skull and the black of the bladder.

The adopted technic included injection of 100 cc of air into the emptied bladder and taking 3 films, 1 in the anteroposterior semierect (40°) position and 1 in each semilateral position with the feet down at an angle of 5° or 10°.

The form of roentgen diagnosis of placenta previa depends upon visualization of the space between the fetal skull and the bladder. Normally, this vesicocranial space is occupied by the bladder wall, peritoneal fold, uterine wall, membranes, and fetal scalp; in placenta previa it is widened by the interposition of some portion of the placenta. Ninety-five per cent of this series were readily interpreted, while with vertex presentations only 3 per cent presented any difficulty. Accuracy is greater in excluding placenta previa than in its diagnosis.

Increased Incidence of Fetal Abnormalities—J. P Greenhill¹⁵ collected data covering 369,597 labor cases and found that whereas the incidence of fetal monsters was 0.94 per cent for the entire group, the frequency of fetal deformities in the 3423 cases of placenta previa in essentially the same group was 275 per If to these 3423 cases are added 1023 cases of placenta previa which he collected from the literature, the incidence of fetal monsters and deformities for the entire group of 4446 cases of placenta previa (representing approximately 4,000,000 obstetric cases) was 25 per cent as contrasted with 094 per cent for all obstetric cases

In approximately half of all the abnormal fetuses associated with placenta previa, the deformity consisted of defects which can easily be recognized by means of x-ray pictures. Hence, in every case of placenta previa, the author suggests, an x-ray picture should be taken. The detection of fetal monsters will usually lead to conservative treatment although cesarean section has to be employed in some cases in spite of the fetal abnormality

Evidence has been presented from embryologists and others to show that great rôle played by environment in the etiology of monsters. Clinical data to support this are obtained from the very high incidence of malformed embryos and twins in cases of tubal pregnancy where the decidual reaction is only slightly developed. Likewise, it is pointed out that the decidual reaction in the isthmus of the uterus is poorly developed and that this plays a rôle in the causation of abnormal fetuses in cases of placenta previa

PREGNANCY

Blood in Pregnancy

Iron Administration and Hemoglobin Levels — E M Widdowson¹⁶ studied the hemoglobin levels of pregnant women before, during and after periods of therapeutic medication with iron Hemoglobin determinations were made by the Haldane method of 100 women, all of whom were 20 weeks' pregnant or less, attending the antepartum department of King's College Hospital, London determinations were repeated a month later Then half the women were prescribed 15 grains (1 Gm) of iron, as ferric ammonium citrate or ferrum reductum, daily for 6 weeks. The level of hemoglobin in the capillary blood was

determined at fortnightly intervals. The administration of iron was then stopped and the hemoglobin estimated fortnightly until a week after delivery.

The other women were given no medicine, and their hemoglobin levels were observed at monthly intervals until delivery and again a week later. In both groups, an estimation was always made within 24 hours after delivery. Thirtyone women were in the "iron" group and 44 in the control group. In the control series the characteristic response was a tendency to fall steadily throughout pregnancy and to rise sharply after delivery. The cause of the fall, although possibly in some cases the result of a true deficiency of iron, is probably due largely to a rise in the volume of plasma unaccompanied by a corresponding rise in the number of circulating red blood cells

The responses of the experimental group are much more complicated than those of the control because, besides the effects of pregnancy and delivery common to the 2 groups, 2 further stimuli were in operation (1) The administration of iron, and (2) the cessation of its administration. The response to iron was not an instantaneous increase in all the women's hemoglobin concentrations A few of the hemoglobin curves continued to fall, as though iron had not been given at all, several showed a break in the fall but no real rise, and some of them rose. The cessation of administration of iron led almost always to a fall in the hemoglobin level of those women in whom its administration had inititated a rise

Breast Cancer and Pregnancy

Influence of Pregnancy and Lactation on Mammary Cancer—H. Bromeis¹⁷ studied 2000 cases of breast carcinoma in relation to pregnancy and lac-

tation and believes that they exert the very opposite effect on carcinoma. Nulliparas and, even more so, women who do not nurse are more liable to the development of mammary carcinoma than others even though the carcinoma in their instance is somewhat less malignant. A large number of childbirths is likely, however, to increase the incidence and the malignancy of a later cancer because of the greater possibility of lactation alterations within the breast

Cancer of the breast rarely develops in the course of a pregnancy but is then unusually malignant, the last months of pregnancy having a particularly unfavorable influence on the neoplasm. An intervening pregnancy likewise exerts an unfavorable influence on the neoplasm. The latter, however, is not nearly as malignant as that which develops in the course of a pregnancy. Mammary cancers arising after childbirth are much more frequent but are less malignant, especially if lactation is practiced.

Lactation appears to have a beneficial influence on the existing mammary can-Malignant transformation of a benigh mammary tumor is particularly frequent in the lactation period. Bromeis was able to demonstrate in experiments on mice that pregnancy stimulates the growth of a caremona and that lactation The incidence of recurrences retards it in animal experiments is lessened when pregnancy takes place shortly after operation. The recurrences arise not during the pregnancy but toward the end of the lactation period. In contrast to this, tumors removed in the course of a pregnancy recur with great rapidity author injected nucleinic acid into tumor mice and obtained the same alterations in their breasts as those observed in pregnancy and lactation These alterations exerted an influence on the growth of the tumor which parallel that of pregnancy and of lactation. These alterations exerted an influence on the growth of the tumor which paralleled that of pregnancy and of lactation. The former stimulated the growth of the tumor and the latter retarded it.

He observed that more than onefourth of the women with mammary carcinoma were of the type presenting marked developmental weakness of the connective tissue. The hormonial influence of pregnancy and lactation was not clear In his opinion a radical operation for mammary cancer without interruption of pregnancy is permissible within the first 2 or 3 months. Provided that an early operation is possible and that the biopsy reveals a tumor of average malignancy. In all other instances a radical operation and interruption of pregnancy are indicated up to the third month. Pregnancy should be interrupted during the fourth and fifth months only when the existing mammary carcinoma is easily operated on and the life of the child is not of any particular importance. From the sixth month on, the interruption of of pregnancy presents no advantage except that in the interest of prolonging the mother's life induction of labor during the seventh month is indicated.

Pregnancy is to be interrupted in all advanced inoperable cases of mammary carcinoma The termination should precede the radical operation by from 2 to 4 weeks. Benign mammary tumors are to be removed at once when observed for the first time during lactation. Castration in pregnant women with mammary cancer is indicated only in the older patients close to the menopause; in younger women it is sufficient to prevent conception for the next 3 to 5 years. Castration is not indicated in cases in which the carcinoma was first recognized during the lactation period. The author likewise feels that sterilization is not to be recommended after a radical operation for mammary carcinoma in a woman during the child-bearing period. It is sufficient here to prevent conception for several years and to keep the other breast under observation during, and especially after, a later pregnancy.

Complications of Pregnancy

Excessive Development of the Human Fetus—The largest baby whose weight was carefully verified was born at the Louise Margaret Hospital in Aldershot, England. As reported by E. L. Moss in 1922 it was the patient's second pregnancy and 5 days before the calculated date she gave birth to a 24-pound 2-ounce stillborn infant.

The occurrence of infants weighing 10 lb. (4500 Gm.) or more at birth is not uncommon At the Chicago Lying-in Hospital during the years 1931 to 1939 there were 20,219 births. In this series, 195 children weighed 10 lb. (4500 Gm.) or more, an incidence of 0.94 per cent. Of these, 177 weighed between 10 and 11 lb. (4500 and 5000 Gm.); 13 between 11 and 13 lb. (5000 and 6000 Gm.); and 1 over 13 lb. (6000 Gm.).

The conditions most commonly causing excessive development of the fetus are prolonged pregnancy or unusually rapid growth of the fetus during a normal period of gestation, but large parents, multiparity, advancing age, and diabetes appear to be contributory factors

A. K Koff and E L. Potter¹⁸ analyze the complications met with in 195 cases of excessive development of the fetus No complications of pregnancy were especially associated with overdevelopment of the fetus except toxemia. This occurred in 27.3 per cent of the women in this study The course of labor in patients with excessive development of the fetus is similar to that in women with generally contracted pelves.

The high incidence of difficult obstetric operations and the number of prolonged labors ultimately ended by cesarean section indicate that the large size of the fetus is frequently missed or that recognition occurs too late for safety.

An abdomen of unusual size, when multiple pregnancy and hydramnios have been eliminated as possible causes, is the most valuable sign of an oversized fetus to the experienced obstetrician This observation, associated with a large unengaged head and inability to impress the head into the inlet of a normal pelvis, should arouse suspicions that the fetus is abnormally large. In multiparas a history of the delivery of one or more large children is of importance If one or both parents are large, if pregnancy is prolonged, and if diabetes mellitus is present in the mother, the probability of excessive development of the fetus is increased

The presence of any of these factors should be an indication for intrauterine mensuration of the fetal head if facilities are available

The obstetric management of patients who give evidence of excessive development of the fetus depends on the degree of disproportion. In patients with contracted pelves, an elective cesarean section is the method of choice

When there is doubt about the degree of disproportion, a test of labor should be given. If the head does not engage within a safe period of time, cesarean section seems to be the best method of delivery. In primiparas where the labor has a greater tendency to be prolonged and where the frequency of serious mechanical intervention and fetal mortality are higher, a shorter test of labor should be given in the interest of both the mother and the child.

Medical induction of labor, particularly when the pregnancy is prolonged,

is frequently successful. The use of Voorhees' bag in artificial rupture of membranes is not recommended by these investigators since these methods increase the incidence of infection and place the mother in great danger should more radical methods of procedure be necessary to effect delivery The authors stress that induction of labor is not justifiable merely because the pregnancy has been prolonged beyond 294 days. It is only when the fetus seems xcessively developed that immediate delivery should be contemplated As a matter of fact, only 1 case of excessive development of the fetus occurs in every 25 pregnancies that have been prolonged beyond 294 days.

Gonorrhea in Pregnant and Non-pregnant Women—Treatment—E J. Bomze, P. G. Fuerstner and F. H. Falls, ¹⁹ report the treatment of 45 cases of gonorrhea in women, 19 of whom were pregnant. They employed a sulfanil-amide derivative (neoprontosil) in doses of 40 grams (2.6 Gm.) daily in 5-day courses. Cure was accomplished in all but 1 patient.

The patients seemed to follow a definite course toward cure after administration of the drug. In most cases the woman reported a marked improvement in subjective symptoms and general well being with a diminution or disappearance of the discharge on the first weekly visit after the medication. Following this the local findings gradually cleared up from week to week. In 3 cases large adnexal inflammatory masses up to baseball size could be felt, gradually decreasing in size on successive weekly visits and finally disappeared entirely in about 4 to 6 weeks. The disappearance of similar masses under other forms of treatment in the same length of time is of course possible, but the authors feel that it is relatively rare that this occurs, and they

would not expect this to happen 3 times in such a small series under other forms of treatment.

Reinfection occurred 14 times in this series, but never while the patient was under active treatment, and always responded promptly to further medication.

Hyperthyroidism Associated with Pregnancy — Diagnosis — B. Portis and H. A Roth²⁰ reviewed the records of 1000 patients of the obstetric department of the Michael Reese Hospital; included also are observations on 500 patients subjected to thyroidectomy in the charity surgical service.

The thyroid gland shows various changes during normal pregnancy Research with human beings and animals directed toward determining the underlying cause has demonstrated the stimulatory effects on the thyroid by the thyrotropic hormone of the anterior pituitary gland

The clinical manifestations referable to the thyroid in normal pregnancy were few. There was frequently an associated nervous instability which simulated hyperthyroidism, however, the accepted physical and laboratory signs were conspicuously absent. It was noted that it was usual to register a normal basal rate during the first 5 months of gestation with an increase of from 15 to 25 per cent later.

The authors encountered hyperthyroidism in 1.4 per cent of 1000 pregnant women and an incidence of pregnancy in 500 patients subjected to thyroidectomy of 0.4 per cent. Fourteen patients evidenced hyperthyroidism in a total of 1000 pregnant women. Ten of the patients were carried to term by conservative measures. Two required thyroidectomy. One was delivered of a stillborn fetus at term, and the fourteenth had an induced abortion at the third month.

The diagnostic features of hyperthyroidism associated with pregnancy were for all intents and purposes identical with those of hyperthyroidism in the nonpregnant state. But the subsequent course frequently assumed a different clinical pattern from that of ordinary hyperthyroidism. It was essential to realize that the accepted progressive nature of thyrotoxicosis was frequently altered during pregnancy The majority of the patients showed either a stationary condition or an amelioration, and only a small number showed progression as gestation continued. Hence it was considered justifiable to observe the individual case for from 1 to 7 months so as to determine the final severity of the thyroid disease Particular attention was placed on the weight, pulse rate, blood pressure and repeated determinations of the basal metabolic rate The patients who showed progression of the thyrotoxic process failed to gain according to the accepted weight curve of pregnancy and many lost weight Further, the basal metabolism showed more marked elevation than that expected because of the physiologic variation already mentioned Finally, the general condition of the patient showed increasing nervousness, irritability and weakness.

Treatment—The prophylactic treatment must take into consideration the avoidance of pregnancy by patients who have evidence of hyperthyroidism or who have manifested thyrotoxic symptoms in previous pregnancies. Antepartum observations of thyroid activity have frequently been helpful in preventing a progression of the disease. The use of iodine early in pregnancy appears well founded, as its use has reduced the incidence of hyperthyroidism.

The active treatment of hyperthyroidism complicating pregnancy has been satisfactory and established. The essen-

tial factor depended on the final clinical pattern which the thyrotoxicosis assumed. The conservative methods of treatment which consisted of adequate rest, sedation and hygienic measures were sufficient in the majority of cases. Compound solution of iodine was frequently advisable as an additional therapeutic agent, but it had to be used judiciously so as not to obscure the progressive character of the disease in some cases. Further, its use might render a patient iodine resistant if surgical intervention was later decided on

Thyroidectomy was necessary for the smaller group of patients, in whom the thyrotoxicosis showed increasing severity, with visceral damage. The period of pregnancy was not the determining factor; however, operation was only occasionally advised in the last trimester. The accepted preoperative treatment with compound solution of iodine and single or stage operations were the accepted procedures, as was the case with thyroid operations in general

Interruption of pregnancy is contraindicated except under unusual circumstances. Some authors, however, still consider that abortion is indicated if the patient is seen in the first trimester and the thyrotoxicosis is mild. Several instances have been reported of thyroid crisis precipitated by such procedures.

Ovariectomy During Gestation— L. Portes and Varangot²¹ state that most surgeons, believing that the early removal of ovarian cysts avoids the complications due to rapid growth, suppuration and torsion, think that "all cysts of the ovary must be subjected to surgery" This essentially prophylactic conception, seems in need of revision on the basis of the present biologic knowledge. Ablation of ovarian cysts is not always indicated because some of them, the follicular cysts for example, must be considered as functional cysts likely to disappear spontaneously. In the course of gestation the prophylactic attitude which favors the ablation of the ovarian cysts appears to have greater justification by reason of the extreme frequency of torsion, which may develop unexpectedly either in the course of gestation or immediately after delivery.

However, there are contraindications to surgical intervention; many of the cysts are purely functional; the lutein cysts, for instance, are relatively frequent in the course of gestation; on the other hand, the effects of ovariectomy on the development of the frequency are uncertain. The authors conclude that it is wise to remove ovarian cysts only when this is necessary on account of mechanical or infectious complications (torsion, hemorrhage, and suppuration). Even in cases in which the intervention is formally indicated, it is advisable to respect the corpus luteum as much as possible, which is easy when it is localized in the healthy ovary, but it is also often possible by dissection or partial resection of the cystic pockets, when it is localized in the diseased ovary. In the cases in which the ablation of the corpus luteum is mevitable, it is advisable to substitute for it, after the operation, by injecting daily and for a long period massive doses of progesterone.

Parovarian Cysts Complicating Pregnancy—A review of 62 cases from the literature of parovarian cysts complicating pregnancy is reported by W Downing and L. O'Toole ²² In systematic fashion the authors discuss the various phases of this subject beginning with embryology.

Parovarian cysts are regarded as resulting from retention of abnormal secretions of the epithelial lining of the parovarium.

The parovarium represents a remnant of the sexual portion of the wolffian body in the female and is a hemologue of the epididymis in the male. It lies in the connective tissue of the broad ligament near the fallopian tube and consists of a main collecting channel, running close and parallel with the tube, together with from 10 to 18 small perpendicular ducts projecting toward the hilus of the ovary.

Parovarian cysts are usually single and unilocular and may be of any size. The cysts are always extraperitoneal or intraligamentary, and the tube lies stretched out over the superior surface of the cyst. A pedicle is not common but one may develop if the cyst grows intra-abdominally, the peritoneal layers of the broad ligament, the tube, the utero-ovarian ligament and even the ovary may be contained in the pedicle. A pedicle was present in 17 of the 62 cases studied in this report.

The cysts are usually pearly gray or pink with thin walls, with the peritoneal layers of the broad ligament freely movable over them owing to their subserous location. The inner surface of the cyst is smooth and glistening, but low papillae may be seen. The fluid is clear and serous and faintly alkaline and contains practically no mucin or pseudomucin. The fluid may be turbid, owing to degeneration and the presence of blood, it is innocuous and suppuration is rare.

During pregnancy the enlarging uterus is usually forced up and out of the pelvis to the side opposite that of the cyst Pain in the back or sides and bladder symptoms are common. At term, the cyst may cause dystocia first by causing an abnormal presentation, second by acting as an insuperable obstacle to the passage of the fetus through the pelvis, and third by producing a rupture of the uterus. A pedunculated cyst may be lo-

cated in any position in the abdomen and not cause symptoms, being only accidentally discovered by the patient or her physician.

Torsion and gangrene of parovarian cysts are common in pregnancy when the cyst has a pedicle, and several such cases have been reported. Gangrene may also result from prolonged pressure during labor. Torsion may develop at any period, but it is most common in the early months of pregnancy and in the puerperium Torsion was a complication necessitating operation in 15 of the 62 cases reported Rupture of the cyst may occur as a result of compression by the uterus and fetal head or of degenerative changes in the cyst wall. Intracystic hemorrhage and suppuration are other less common complications Premature separation of the normally implanted placenta has been reported in a case of parovarian cyst.

The differential diagnosis of parovarian from ovarian cysts during pregnancy is usually not possible.

Treatment — The indications for treatment of cysts encountered during pregnancy vary with the period of pregnancy and the size and location of the cyst If a diagnosis of parovarian cyst is made in a patient seen during the first half of pregnancy, the cyst should be removed as early as possible if it is large, particularly if it is situated low in the pelvis and is not movable. If it is small, the patient may be kept under close observation and if it does not enlarge its removal may be postponed until after the termination of the pregnancy. Torsion of the cyst, however, may occur at any stage of pregnancy and necessitate an immediate operation.

During the second half of pregnancy the cyst, if large and fixed in the pelvis, should be removed at once, if small and not incarcerated, the patient may be

watched closely and operation may be delayed at least until the fetus becomes viable. A study of the 62 cases in this report indicates that in the majority of patients the cyst enlarges, often rapidly, during pregnancy.

If a parovarian cyst is not diagnosed until labor is imminent or in progress, several procedures are possible: First, an attempt should not be made to do a forceful delivery alongside the cyst if it is large and prevents the fetal head from entering the pelvis Second, reposition of the cyst under anesthesia with the patient in the Trendelenburg position may be attempted. If the cyst origmates in the broad ligament with no pedicle this will rarely be possible, but it may be successful if it is of ovarian origin. Third, if the cyst is incarcerated in the pelvis it may be aspirated through the posterior vaginal wall, a blunt needle being introduced close to the posterior edge of the cervix in the median line During the puerperium the cyst should be removed by laparotomy, since the flabby cyst is apt to undergo torsion if it has a pedicle

In suitable cases in which aspiration is not advisable because of the danger of mjuring the vessels or ureter or because of the maccessibility of the cyst, a cesarean section should be performed, followed by extirpation of the cyst when the condition of the patient permits Λ few authors advise against treatment by aspiration, but that procedure is much safer than section in most hands and it seems to us that it is the method of choice when the cyst is incarcerated below the uterus. The removal of the cyst following cesarean section is often difficult if it is deep in the broad ligament or if an inflammatory reaction is present In an occasional case in which infection of the cyst or uterus is present, a total hysterectomy is indicated following the cesarean section.

Abortion or premature labor rarely results from laparotomy and removal of the parovarian cyst, even when torsion necessitates an immediate operation. The most favorable period during pregnancy for intervention seems to be the fourth month.

Pneumococcic Pneumonias Complicating Pregnancy and the Puerperium—A series of 212 cases of typed pneumococcic pneumonia complicating pregnancy and the puerperium which occurred at the Boston City Hospital and the Boston Lying-in Hospital was analyzed by M. Finland and T. D. Dublin^{2,3} with respect to the more important features concerning both the pneumonia and the pregnancy

Pneumonia complicating pregnancy concerns the obstetrician because of the high maternal and fetal mortality which it entails, and it concerns the internist because it carries with it a considerably higher death rate than pneumonia in nonpregnant women. It accounts for about 1 death in every 5000 deliveries and is the cause of about one-half of the maternal deaths that are due to nonobstetric causes. Early and adequate treatment with the homologous typespecific antipneumococcus serums can be expected to reduce materially the high death rate from the pneumomas when they complicate pregnancy

The higher death rate and particularly the higher incidence of bacterenia in the cases of pneumonia complicating pregnancy are definite indications for larger doses than are used for nonpregnant patients. These larger doses have been recommended in the Massachusetts pneumonia control program and were used in the present cases. As much as 1400 cc. of unconcentrated Type 1 serum was given in some of the earlier cases in this

series. The average dose in the recent cases was more than 250,000 units, which is higher than that used in other patients of the same age groups.

It is too soon to evaluate the place of chemotherapy in the treatment of pneumonia. There is no doubt that the use of **sulfanilamide** has materially reduced the death rate from hemolytic streptococcus infections, which are responsible for most puerperal sepsis. That this drug may favorably influence streptococcic pneumonia is to be anticipated. although there is no convincing evidence so far that it does. The drug is known to enter the fetal circulation and the mother's breast milk, but its influence on the baby or the fetus has not yet been determined. There is no good evidence that sulfanilamide itself has curative value in the treatment of severe pneumococcic pneumonias. Other derivatives, such as sulfapyridine, may prove to be very useful, but there are good reasons for the belief that the greatest benefits from these drugs in the treatment of pneumococcic pneumonias will be obtained from their use in conjunction with specific antipneumococcus serums.

The death rates were highest for late pregnancy and for women whose pregnancy was terminated during the disease. The death rate for all the serum-treated patients was almost one-half of that for the corresponding nonserum-treated patients. The lower death rates were for pneumonia complicating both early and late pregnancy, for postpartum pneumonia, for women who were delivered and those whose pregnancy was unaffected

The frequency with which pregnancy was terminated did not seem to be influenced by serum treatment.

Pyelitis—Ureteral Catheterization—During a period of 4 years V. W. Dix and H. Evans²⁴ state that 84 cases of

pyelitis of pregnancy were admitted to the London Hospital, and of these only 7 required ureteral drainage, 5 because of failure to respond to alkali therapy and 2 because of excessive vomiting, making the administration of alkali impossible. Nine ureteral catheterizations were carried out. In 1 instance the second catheterization was necessary because the first catheter was removed by a nurse when the patient returned to the ward, and in another the second catheterization was performed 3½ months after the first during a recurrence of pyelitis. In no case was it necessary to use an anesthetic.

Catheterization of the ureter during pregnancy is not easy and should be carried out only by the expert. If it should ever be necessary for the relatively inexpert to attempt catheterization in the later stages of pregnancy, an anesthetic should be given to minimize the difficulties. When the ureteral orifice has been identified and the catheterization has begun there should be no difficulty, and the fact that the catheter has reached the renal pelvis will be at once evident from the rapid flow of urine, which is considerably in excess of that from a ureteral catheter of the same size passed into a normal pelvis. In cases in which there has been a complete block at the pelviureteral junction the flow may be rapid.

It is advisable to pass as large a catheter as possible The sizes used have been 10 and 12 Great care must be taken, in withdrawing the cystoscope, to avoid displacement of the catheter The catheter is attached to the leg and the urine is allowed to drain into a bottle. The catheter was usually left in place for 3 or 4 days. However, equally good results might be obtained if the catheter remained in place for only 1 or 2 days, although there would perhaps be a

slightly increased risk of recurrence. It should be removed at once if urine ceases to run freely and gentle syringing fails to re-establish the flow. The effect of catheterization and drainage alone on the 7 patients was so good that no additional treatment was needed except the continued administration of citrate. Premature induction of labor should rarely, if ever, be necessary, even in severe pyelitis of pregnancy. One case of postpregnancy pyelitis was also treated successfully by catheterization.

Syphilis—M. A. Castallo, J. A. Coppolino, A E Rakoff, P. H Roeder and G. S. Dickson²⁵ treated 116 syphilitic pregnant women with mapharsen and bismuth. Twenty-six were primigravidas, none of whom had received previous treatment. Among the multigravidas, 22 had received treatment in earlier pregnancies Treatment consisted of weekly intravenous injections of 40 mg of mapharsen and intramuscular injections of bismuth salicylate in oil. A total of 849 injections containing 31,940 mg of mapharsen was given. There were 106 live births for the entire group. Among 76 patients who received 6 or more treatments there were 72 live births There were only 41 live births among 49 patients who started treatment before the sixth lunar month. There were 10 fetal deaths, 7 being stillbirths and 3 miscarriages These mothers received from 1 to 10 treatments, the average being 5 Fifty of the 106 babies born alive have been followed in the pediatric clinic. Five proved to be Wassermann positive

Nausea and vomiting following the first few injections occurred in almost every woman. Persistent gastrointestinal reactions were frequent, occurring in 66 of the group In 6 instances these were so severe as to necessitate withdrawal of the drug. Relative or actual

loss in weight was common. The results are compared with those obtained in similar groups of patients who had been treated with neoarsphenamine, acetylarsan and quinine iodobismuthate, and the authors believe that neoarsphenamine is the drug of choice for the treatment of syphilis complicating pregnancy.

Laws Requiring Premarital and Pregnancy Tests for Syphilis—Reasons for and against laws requiring premarital and pregnancy tests for syphilis are analyzed by J. A. Kolmer ²⁶ Briefly the reasons for the legal requirements of premarital blood tests for syphilis are summarized as follows:

- 1 Because marriage inevitably involves syphilitic men and women in view of the high incidence of the disease
- 2 Because legally required premarital blood tests will tend to lower the incidence of syphilis
- 3 Because blood tests are the most valuable single means for the detection of the disease, especially after the primary, or chance, stage
- 4 Because of the madequacy or absence of a history of infection
- 5 Because of the madequacy of clinical detection of the disease
- 6 Because premarital blood tests will reduce the incidence of transmission of syphilis to spouse and children
- 7 Because premarital blood tests reduce the incidence of the economic hazards of marriage from incapacity or early death of the spouse
- 8 Because premarital blood tests will reduce the incidence of divorce.
- 9 Because premarital blood tests will greatly encourage the thorough treatment of syphilis
- 10 Because premarital blood tests are an excellent phase of the educational program against syphilis

The reasons against the legal requirement of premarital blood tests for syphilis are summarized as follows:

- 1 Because premarital blood tests may give nonspecific or falsely positive reactions.
- 2 Because positive blood reactions as the only evidence of syphilis may not always indicate a danger to marriage, especially in the case of thoroughly treated chronic syphilis.

- 3. Because the legal requirement of premarital blood tests may discourage marriage and promote sexual promiscuity.
- 4. Because premarital blood tests alone may not detect syphilis especially in its incubationary and primary stages.

The reasons for the legal requirement of blood tests for syphilis during pregnancy or at delivery are summarized as follows:

- 1 Because blood tests during pregnancy afford an excellent opportunity for detecting syphilis in both married and unmarried women.
- 2 Because the detection and treatment of syphilis in pregnancy increases the chance of the birth of a nonsyphilitic child, with a reduction in the number of miscarriages and in infant mortality.
- 3 Because the detection of syphilis in pregnancy results in the treatment of the mother, especially during subsequent pregnancies.
- 4 Because the detection of syphilis in pregnancy may result in its detection and treatment in the child after birth.
- 5 Because the detection of syphilis during pregnancy may lead to its detection and treatment in the father and other children.

Dietary Requirements in Pregnancy

These are critically reviewed by W J Dieckmann and W W. Swanson.²⁷ Certain dietary demands must be met to protect both mother and offspring from clinical pathologic changes during pregnancy

Although pregnancy under normal conditions is essentially a physiologic process, it makes special demands on the maternal organism, and diets adequate under ordinary conditions may fail to meet the increased requirements. Many of our concentrated foods are low in vitamins, residue and alkaline minerals and high in carbohydrates and acid minerals. The foods that correct deficiencies common to our diet are milk, eggs, and leafy vegetables. These protective foods are highly essential during pregnancy and can prevent maternal and

fetal morbidity due to demineralization and avitaminosis.

The average increase in weight during pregnancy amounts to 9.7 kg. with a standard deviation of 4.3 kg. The authors have attempted to restrict the total weight gain to approximately 7.5 kg. (16.5 pounds) or a maximum weekly gain of 225 Gm. (0.5 pound). Efforts to control the size of the fetus near term by low Caloric intake are generally unavailing and may do considerable harm if essential food constituents are withheld.

The Foods in Pregnancy—Carbo-hydrates—In pregnancy when nausea and vomiting occur, it is advisable to give a high carbohydrate diet every 2 hours. When severe toxemia of pregnancy is present or imminent, Dieckmann suggests the use of an eclamptic diet which consists of only fruits and sweetened fruit juices

Protein—The nitrogen requirement during pregnancy for growth of the ovum, the uterus and mammary glands is about 135 to 145 Gm. From extensive studies of serum proteins, Dieckmann found that only those patients with obvious nephrosis have had a low serum protein. He states that the serum protein concentration in normal pregnancy is 6.4 Gm. per cent with a standard deviation of 0.4 Gm per cent, and in preeclamptic patients, the average is 6.0 Gm per cent; in the vascular renal group, 6.6 Gm. per cent; and in eclampsia, 6.7 Gm per cent.

Fat—Fat appears to be of primary importance as a carrier of essential vitamins A, D, E and F.

Fluids—The authors believe that sufficient water should be ingested to ensure a normal urmary output of 1200 to 1500 cc. per 24 hours.

Inorganic Constituents in Pregnancy—Calcium—It appears probable

that all cases of fetal rickets due primarily to mineral deficient diets during pregnancy, would show hypomineralization. With respect to the mother, the first few infants born may not suffer to any extent, but Dieckmann has shown that frequent pregnancies and deficient nutrition have a cumulative effect. The calcium and phosphorous requirements of the mother in pregnancy are best satisfied by an intake sufficient to produce positive balances. Dieckmann, basing his statement on balance studies of patients suffering from a calcium and phosphorous deficiency, advises that the diet in pregnancy contain at least 22 grains (1.5 Gm.) calcium and 30 grains (2.0 Gm.) phosphorus. Certain conditions may affect the optimum retention of calcium and phosphorus such as the percentage utilization of these minerals from the ingested food, the therapeutic administration of vitamin D and the effect of sunlight or irradiation with ultraviolet light

The foods rich in calcium are milk of animals and leafy vegetables. Apparently the best sources of calcium and phosphorus are milk and cheese. A quart of milk contains approximately 18 grains (1.2 cm.) of calcium and 14 grains (0.9 cm.) phosphorus. The leafy vegetables contain considerable calcium but the presence of oxalates forming insoluble salts lowers the percentage that can be utilized.

It is apparent that at least 1 quart of milk daily is necessary to bring the calcium intake up to the required limits. As substitutes it would take approximately 5 ounces (150 Gm.) of cheese or 12 average size oranges to have the same calcium content. Calcium salts, whether in the form of gluconate, lactate, or perhaps the best, dicalcium phosphate, are more expensive than milk and are usually excreted almost quantitatively in the urine and feces. It would require some

2 drams (8 Gm.) daily of dicalcium phosphate, because of the uncertainty of utilization, to equal the amount obtained from 1 quart of milk.

Iron—The studies on iron metabolism in pregnancy indicate depletion of maternal stores with successive births. An average maternal intake of \(\frac{1}{4} \) grain (15) mg) of iron a day permits an average retention of $\frac{1}{20}$ grain (32 mg), sufficient to provide for the calculated needs of the mother and fetus. The foods rich ın assımılable iron are liver, kidney, gızzards, red meats, raisms, prunes, apricots, and peaches. Iron salts and the vitamin B complex may be used to supplement the maternal diet, but their value is very questionable. Where the anemia is marked, transfusions of blood are ındicated

Vitamins in Pregnancy-Vitamin **B**—With respect to pregnancy, the interest in the fractions of the B complex is in B_1 , thianin, the antineuritic factor, and the B₂ complex Polyneuritis may occur, whatever the previous condition or diet, if there is severe vomiting of pregnancy. In districts where pellagra is prevalent, the increased need of vitamm B₂ complex in pregnancy may unmask the latent disease. The food sources of the vitamin B complex are yeast, whole grain breads, and oils, cabbage, and carrots, leafy vegetables, egg yolk, and oysters. To supplement these foods there are a number of concentrated vitamin B complex extracts besides the isolated vitamin B fractions available

Vitamin D -- The administration of vitamin D, calciferol, in pregnancy is not a routine procedure in obstetric practice. However, the giving of therapeutic doses of vitamin D as found in cod-liver oil and in concentrates, or exposure to sunlight is a most justifiable measure. Careful search of the literature seems to indicate that in the infant a correlation may exist

between calcium deficiency, premature births, imperfect calcification, and birth trauma.

It should be emphasized again that supplementing the diet of the mother with therapeutic doses of vitamin D from fish oils, concentrates or from the action of sunlight on the skin does not permit a decrease in the daily optimum calcium and phosphorous intake. Pregnant women should be given a teaspoonful of good grade cod-liver oil, 350 to 400 International Units, daily, or the gradual exposure to sunlight or irradiation with ultraviolet light sufficient to maintain a slight tan.

Vitamin E—Vitamin E appears to be of most importance in pregnant women subject to habitual abortion. Many potent concentrates are on the market. In its natural state, E is found mostly in whole grains, egg yolk, green vegetables, and muscle meat.

Foods in Lactation—The production of milk in the lactating mother does not require any expenditure of energy other than that contained in the milk itself, which in the human amounts to 700 Calories per 1000 cc Restricted muscular activity, freedom from worries, sufficient sleep, and an adequate diet promote milk secretion All foods are needed in more abundance However, the ingestion of foods rich in carbohydrates does not appear to augment the yield of milk but tends to increase the fat content intake of foods rich in fat increased slightly the volume of milk with considerable increase in the concentration of fats.

The restriction of fluid intake may limit milk yield when all other necessary constituents are supplied in ample amounts. If the patient is able to obtain a properly balanced diet containing milk, butter, eggs, meat, fruits and vegetables, the authors do not prescribe any vitamins. It is not, they state, so much the actual amount of protein, calcium, phosphorus, 170n, iodine, etc., in the diet as their assimilability by the patient. Although deficiencies in diet causing morbidity of the fetus, such as rickets, hypoplasia of the teeth, tetany, and anemia, may be corrected in early infancy, yet the first opportunity has been lost in not preventing the condition before it had a chance to develop.

Hydatid Mole

Diagnosis and Treatment of Hydatidiform Mole and Chorioepithelioma—An analysis of the extensive papers written prior to 1930, including about 1500 cases of chorioepithelioma and probably 10 times as many moles, shows that the mortality rate of mole was approximately 12 per cent and that of chorioepithelioma 60 per cent. A review of the world's literature for the last 3 years, involving 576 cases of mole and 266 of chorioepithelioma, shows the mortality rate now to be approximately 2 per cent and 10 per cent, respectively.

Although all authorities agree on the value of the biologic pregnancy test in the diagnosis of mole and chorioepithelionia when only qualitative tests are used, A Mathieu²⁸ warns that one must be aware of the following facts.

(1) The test is positive in the presence of living chorionic tissue, which includes normal pregnancy, (2) the test is also positive in hydatidiform mole, chorioepithelioma, or metastases of either disease; (3) the test may be negative in missed molar abortion, (4) the test may be positive for 6 weeks following the passage of a mole because of stored hormone in the body, (5) if a test is positive 2 months after the passage of a mole, and normal pregnancy has been excluded, it is likely that living molar tissue is still present or chorioepithelioma has developed; (6) in the presence of lutein cysts after all living chorionic tissue has been removed, the test will be positive until these cysts regress because the hormone is stored in them, (7) a positive test 1 month after the

removal of a chorioepithelioma is strong evidence of metastasis; (8) the spinal fluid gives a negative test in normal pregnancy and a positive test in mole or chorioepithelioma; (9) absolute reliance should not be placed on 1 test, and in questionable cases the test should be checked and rechecked, (10) the test should be used in all questionable conditions where the elements of chorioepithelioma might exist; and (11) the biologic test should overrule contrary clinical and pathologic findings.

There is a suggestion that some lytic substance might possibly be evolved as a This is based on the fact that approximately 80 per cent of pregnant women have living chorionic cells in the circulation, and that after delivery a lytic substance is present in their blood which destroys the chorionic tissue, that is, serum of normal women during pregnancy is able to destroy migratory chorionic cells, while serum from women with chorioepithelionia does not seem to possess this lytic action. The lack of this substance is held to be responsible for the almost 100 per cent mortality in teratomatous chorroepithelioma of the ovary and the testicle. It has been recommended that selected patients with hopeless chorioepithelioma be treated by intravenous administration of large doses of serum from the pregnant human female, and if the reaction is favorable that serum from one of the lower animals, such as the mare, be investigated.

Multiple Pregnancy

Maternal and Fetal Expectations-

The subject of multiple pregnancy is discussed by J. C. Hirst ²⁹ Maternal, fetal and neonatal deaths associated with twin and triplet pregnancy have been analyzed from 223,394 total births over 16 weeks' gestation in Philadelphia from 1931 to 1937 inclusive; and detailed maternal and infant progress from 4 sets of triplets and 305 pairs of twins from

the Lying-in, University, and Preston Retreat Hospitals has been analyzed.

Maternal, stillbirth, and neonatal death rates from twin pregnancies have been shown to be increased roughly about 3 times over those for single births

The author suggests abdominal tension resulting in renal ischemia or ureteral obstruction as a common factor in both nulliparous "low reserve kidney" and "mild preeclampsia" in multiple pregnancy.

Quantitative serum and 24-hour urinary excretion of estrogen and prolan should determine whether "low reserve kidney" and many cases of multiple pregnancy toxemia are similar, and distinct from preeclampsia

By becoming twin conscious, three-fourths of all multiple pregnancies may be diagnosed manually, and 90 per cent of suspected cases should be diagnosed by x-rays in time to provide dietetic, tonic, and physical support, avoidance of unnecessary cesarean section, and excess sedation and ether in labor, and hospitalization including preparation for immediate transfusion in all cases, thereby reducing both maternal and fetal accidents by at least one-half

More time up to 1 hour, and fewer versions are indicated for the second birth, to allow opportunity for the uterus to readjust itself, thereby numinizing the risk of infection and postpartum hemorrhage

Scrupulous management of the third stage of labor, and uterine packing for 8 hours in all cases of hemorrhage before or after delivery will prevent many deaths from twin births.

Prematurity is the greatest infant hazard, prejudicing the neonatal period more than the natal.

Meticulous care, including microscopic examination, in examining the secundines

from multiple pregnancy should be obligatory.

Pelvic Measurements

Pelvic Inlet Variation in 400 Negro Women — Richard Torpin and L. P. Holmes³⁰ state that external pelvimetry is of so little value that they believe the time has come when it can be discarded. The estimate of the constitutional type of the patient is of far greater value in prognosis of labor. Women of slender and medium constitutions as a rule do well. Those giving most trouble in labor are the overweight, heavy-featured type, with male distribution of hair. These are inclined toward the Froehlich type, the dystrophia dystocia syndrome and, in addition to a tendency to possession of rarer types of pelvis and a predilection for occipitoposterior presentation of the fetal head, have painful but ineffective uterine contractions, possibly associated with hormonal disturbances. Of all methods of study of the obstetric pelvic short of roentgenography, the most valuable the authors maintain is estimation of the conjugata vera by subtracting $1\frac{1}{2}$ to 2 cm from the measured conjugata diagonalis. Criticism has been made that the promontory cannot be palpated in all patients When that occurs, the diameter is usually large enough. In all cases of contraction in which the conjugata vera was 9 cm or less, the authors have been able to estimate it within 05 to 1 cm. as checked by the x-ray "grid" method. Palpation of the contour of the ischial spines and the subpubic angle gives a fairly good estimate of the outlet

Clinical Significance of Pelvic Variations—H. Thoms, W R. Foote and I. Friedman³¹ discuss their results with routine roentgen pelvimetry.

The method which is briefly outlined in this communication is simple, rapid, and inexpensive, and, during the past 4 years, it has been used routinely in primigravid patients.

The important planes and dimensions of the obstetric pelvis are described by the authors as follows:

From the obstetric viewpoint, there are 3 portions of the pelvis concerning which information is important. These are: (1) The plane of the pelvic inlet; (2) the midpelvic or narrow pelvic plane, and (3) the planes of the pelvic outlet.

1. The plane may be described as follows: It is bounded anteriorly by the upper posterior surface of the symphysis, laterally by the ilhopectineal lines, and posteriorly by the upper anterior surface of the sacrum at the point where the iliopectineal lines would meet if they were to be continued posteriorly. In the individual pelvis this point may or may not be located at the promontory. It is usually somewhat below this process.

In addition to a knowledge of the shape of the plane of the pelvic inlet, there are 3 diameters which furnish useful information: (1) The anteroposterior diameter, (2) the transverse diameter, and (3) the posterior sagittal diameter

The anteroposterior diameter extends from a point on the upper posterior surface of the symphysis about 1 cm. below the superior border to the anterior surface of the sacrum at the point where the iliopectineal lines would meet if they were to be continued.

The transverse diameter is the greatest distance separating the iliopectineal lines. It bisects the anteroposterior diameter somewhat posterior to its midpoint

The posterior sagittal diameter is that portion of the anteroposterior diameter which is posterior to the point of intersection by the transverse diameter. It is useful as an index of the amount of space in the upper posterior pelvis. When abnormally shortened, it represents an ab-

normal posterior displacement of the transverse diameter.

2. The Midpelvic or Narrow Pelvic Plane—The plane is also known as the plane of least dimensions and is defined as extending from the lower border of the symphysis laterally through the ischial spines, then posteriorly to the juncture of the fourth and fifth sacral vertebrae.

The anteroposterior diameter of the midpelvic plane, therefore, extends from the lower border of the symphysis through the bispinous diameter, and usually to the junction of the fourth and fifth sacral segments.

The transverse diameter of the narrow pelvic plane, also known as the bispinous diameter, is the shortest distance separating these projections

The posterior sagittal diameter of the narrow pelvic plane is that portion of the anteroposterior diameter which lies posterior to its intersection by the bispinous diameter. This diameter gives a useful index to the available space in the posterior lower midpelvis and its length is modified by the size and shape of the greater sacrosciatic notch.

The Pelvic Outlet — The pelvic outlet consists of 2 planes represented by 2 triangles, the bases of which join along the line of the bituberal diameter anterior triangle is bounded laterally and above by the bones comprising the pubic arch The posterior triangle is bounded anteriorly by the bituberal diameter and its sides converge posteriorly to the tip of the sacrum. The important diameters of the outlet are the bituheral or transverse of the outlet, representing the widest separation of the lower inner surfaces of the tubera ischii and the posterior sagittal diameter which extends posteriorly from a midpoint on the bituberal diameter to the anterior surface of the tip of the sacrum.

The method used for routine pelvimetry is described as follows:

The pelvic inlet may be visualized and measured by the centimeter grid method of roentgen pelvimetry. This consists of the projection of the pelvic inlet to the sensitive film with the patient in a semirecumbent position and the target at a 30-in. distance. Distortion due to the spread of the rays is corrected by the perforated centimeter grid which is placed in the plane of the pelvic inlet following the exposure and removal of the patient from the table. A second (flash) exposure reproduces small dots on the film, the distance between which represents centimeters in the plane of the inlet. All of the pelvic inlet diameters may be read directly In addition, the outline of the inlet may be visualized as well as the side walls of the lower pelvis and the ischial spines. The distance between these processes (bispinous diameter) is also measured on this film, using a distortion table to correct spread of the rays for the level in which they rest. This level is determined in the lateral film

The second roentgenogram depicts the lateral aspect of the pelvis and is taken with the patient standing laterally to the target which is placed at 5-foot distance. Distortion due to the spread of the rays is corrected by means of an opaque centimeter notched rod which is placed posterior to the patient and in the midplane of the body. A corrected scale is thus projected on the edge of the film and with calibers all of the anteroposterior diameters of the pelvis may be measured On this film, therefore, they measure the anteroposterior diameter of the inlet, the anteroposterior diameter of the narrow pelvic plane, the posterior sagittal diameter of this plane, and the posterior sagittal diameter of the outlet Also, in the lateral film they may visualize all of the important lateral contours

of the pelvis, including the sacral curve and the character of the sacrosciatic notch.

For the determination of the intertuberal or transverse diameter of the outlet, they depend upon palpation and direct measurement. The contour of the lateral aspects of the pubic arch are also described after palpation. For routine purposes they have found these outlet palpatory methods quite as satisfactory as roentgenometry of this portion of the pelvis.

Studies in this clinic have shown that for practical obstetric purposes, female pelves may be divided into 4 general groups using the shape of the pelvic inlet as a basis for classification.

- 1 Dolichopellic or anthropoid type— The anteroposterior diameter exceeds the transverse diameter, the pelvis being elongated anteroposteriorly.
- 2 The mesatipellic or round type— The anteroposterior and transverse diameters are of equal length, or the transverse exceeds the anteroposterior by not more than 1 cm
- 3 The brachypellic or oval type—The transverse diameter exceeds the anteroposterior diameter by more than 1 cm. and less than 3 cm.
- 4 The platypellic or flat type—The transverse diameter exceeds the anteroposterior diameter by 3 cm or more

The authors re-emphasize their previous dictum that the most favorable type of pelvic inlet is that which is round or which is elongated anteroposteriorly (mesatipellic or dolichopellic), and not the transversely oval pelvis (brachypellic).

Tests for Pregnancy

Biologic Pregnancy Diagnosis Tests—F. A. E. Crew³² compared the biologic pregnancy tests and asserts that the *Hogben test* (using the toad Xeno-

pus laevis) can replace the Friedman rabbit test but not the Aschheim-Zondek mouse test. The toad can give a trustworthy positive result within 6 to 15 hours, as compared with the 24 to 48 hours needed if the rabbit is used. The toad is better than the rabbit for use in those cases in which a definite positive or an emphatic negative is the answer, especially when the result is urgently required With the present methods of preparation, however, the toad does not give the graded results yielded by the mouse. It may be shown later that differences in the number of eggs extruded are indeed true reflections of corresponding differences in hormone concentration, but for the present the mouse must be retained.

Toxemia of Pregnancy

Etiology and Treatment of Hyperemesis Gravidarum — E Bandstrup³³ sums up present knowledge by stating that, owing to some unknown cause, the woman begins to vomit. The further course of the illness may depend to a large extent on psychic factors A state of manition develops, of which want of glycogen in the liver is probably the most serious feature even though the want of salt, water and vitamins, together with the development of acidosis, is an important factor A specific toxin of hyperemesis has never been demonstrated as a cause of the necrotic changes in the liver and other organs, and it is not inconceivable that these changes may develop as a result of the manition under the special endocrine conditions present in pregnancy

In keeping with his view of the pathogenesis of this disease, his treatment consists of a firm suggestive management on the part of the physician and admission to a hospital, possibly with isolation of the patient. Sedatives, such

as bromides and barbituric acid, have a calming effect on the mind of the patient and lower the irritability of the center for vomiting. The restorative therapy consists in the administration of dextrose, insulin, sodium chloride, water and vitamins. The future will show whether adrenal cortex extract is to be established as an effective remedy in the restorative therapy. If conservative treatment on these principles fails to lead to recovery, it may be necessary to induce abortion.

Seven symptoms are considered as indications for interruption of pregnancy in hyperemesis. These symptoms include elevation of the temperature above 100 6° F. (38.1° C), or persistent subfebrile temperature, persistent increase in the pulse rate over 100 a minute, jaundice, albuminuria, polyneuritis, ocular symptoms, and psychotic changes

From a study of 40 fatal cases of hyperemesis, 25 presented only 1 or more of the foregoing serious symptoms for more than 1 week prior to interruption of pregnancy or death. So the mere presence of 1 serious symptom has to be taken as a warning. Therapeutic abortion in 30 of the 40 cases was performed

G Guhr³⁴ reports the results obtained in 12 cases of hyperemesis gravidarum which were treated with *vitamin* B_1 and liver preparations The patients are given intragluteal injections of ampoules of liver extract (22 cc) which contain 500 International Units of vitamin B₁. At first, 1 ampoule of the preparation is injected daily and as soon as improvement is noticeable the injections are given every second day. The total number of injections varies in different cases, but from 6 to 10 are usually sufficient. In especially severe cases more than 1 injection may be given daily The diet should be rich in carbohydrates.

Discussing the mode of action of the combined administration of vitamin B₁ and liver, the author suggests that it acts as a protective liver therapy, because investigations indicate that a primary hepatic disorder and the involved disturbance in the carbohydrate metabolism are decisive factors in the genesis of hyperemesis gravidarum. Dysfunction of the anterior lobe of the hypophysis is the eliciting cause. Deficiency in vitamin B₁ is not regarded as a causal factor of hyperemesis gravidarum; however, as an adjuvant vitamin B₁ supports the action of the liver extract in that it not only favors an increase in glycogen but also normalizes the disordered carbohydrate metabolism

Eclampsia—Laboratory Findings
—An analysis of some laboratory findings in 90 cases of eclampsia is presented by L. C. Chesley 35

Blood Uric Acid—The absolute level is often elevated in eclampsia. More generally, the ratio of uric acid to nonprotein nitrogen is increased. The upper normal ratio is about 10 per cent.

Urinary Specific Gravity— The attainable concentrations of the urine is markedly reduced, not by eclampsia usually, but by the prophylaxis and treatment of the disease.

Urea N/Nonprotein Nitrogen—This ratio varies with the urine volume output and tends to decrease in normal pregnancy. As a measure of renal function, it is nonspecific and, in toxemia especially, is unreliable

Phenolsulfonephthalem — In eclampsia and in pregnancy generally ureteral dilatation may be so marked that in spite of a normal renal excretion of dye, the test seems to give subnormal results. The dye may be excreted, but stagnating in the ureters, it is not available for analysis.

Urea Clearance—In the authors' opinion, the urea clearance is unaffected in pregnancy and is normal in eclampsia. unless there is a concomitant renal disease. Urea clearances, if calculated as standard clearances, are grossly erroneous when the urine volume output falls below about 0.35 ml. per minute. The calculated standard clearance, as well as the maximal clearance, is independent of the urine volume output (above 0.35 ml/min). It is also independent of the blood urea and of factors influencing the blood urea, such as tissue binding or tissue release of urea When marked hemoconcentration occurs, the clearance may be low because of this extrarenal factor.

Anterior Pituitarylike Hormone in Late Pregnancy Toxemia - George Smith and O W. Smith³⁶ present their criteria for normal levels of the gonadotrophic factor in pregnancy based upon their analyses of 210 serums from 64 patients who were normally pregnant and continued so to delivery. In 36 of these cases, serum assays were performed at intervals from as early as the sixth week of gestation to delivery The rest were studied by single specimens during the last trimester A peak in the curve of the anterior pituitarylike hormone in both the serum and urine has been found by these investigators to occur at about the time of the second missed period, the values at this time being frequently as high as or higher than those observed in cases of chrorionepithelioma or hydatidiform mole. This high level, however, is maintained for only a comparatively short time, 1 to 3 weeks, a fact which supplies an important means of differentiating between early pregnancy and mole. By the beginning of the fourth month the anterior pituitarylike hormone of serum and urine has reached a constant low

level and in no instant of normal pregnancy between the fifth and eighth months have the serum values been higher than 100 R.U. per 100 cc. During the last 4 weeks of gestation in a number of cases the serum anterior pituitarylike hormone rose somewhat above this amount. Values above 100 R.U. per 100 cc. prior to the fifth missed period or within 4 weeks of term are therefore not considered abnormal.

Abnormally high levels of A.P.L. hormone in the serum of patients with late pregnancy toxemia and eclampsia were first reported by the authors in 1933. The total data of the past 7 years of this study are summarized as follows.

- 1. Preeclamptic toxemia and eclampsia are usually (88 per cent in this series) characterized by the finding of excessive amounts of anterior pituitarylike hormone in the serum. This excess has been found to precede clinical signs by 4 to 6 weeks.
- 2 In a small percentage of cases with a clinical diagnosis of preeclampsia or eclampsia, the serum anterior pituitarylike hormone does not exceed normal levels
- 3 In patients quite definitely diagnosed as nephritic or hypertensive (symptoms beginning earlier in pregnancy), the serum anterior pituitarylike hormone is normal.
- 4 Premature delivery may or may not be associated with excessive anterior pituitarylike hormone.
- 5 The finding of high levels of this substance in the serum during the fifth, sixth, or seventh months warrants the prediction of impending preeclampsia or premature delivery

The technic of these investigators is as follows

Technic — At 2 to 3-week intervals between the fifth and eighth months of pregnancy, 10 cc of venous blood are collected without any anticoagulant and the clot allowed to form. The serum is separated, cleared of any cells by centrifugation and measured accurately into 4 15 cc centrifuge tubes, each tube to contain 10 cc, 05 cc, 05 cc., and 0.3 cc, respectively. About 10 cc. of 95

per cent ethyl alcohol are added to each tube, the contents mixed and the tubes placed in the refrigerator for 12 to 18 hours. After centrifuging and pouring off the supernatant alcohol, the precipitate is washed (stirring rod and shaking) once with ether, approximately 12 cc., and again centrifuged. The ether is then poured off and the tubes allowed to drain for a few minutes, after which 3 cc. of normal saline is added and mixed with the precipitate, forming a smooth emulsion. The other held back by the precipitate and saline is removed by stirring the contents up onto the sides of the centrifuge tubes while rotating, warming with the hand and blowing into (No more heat than this the tubes. should be applied—to avoid the possibility of any destruction of the hormone.) The stirring rods are washed down with 3 cc of saline, making the total content of each tube 6 cc, this being the final test solution.

Each extract is administered subcutaneously into a 19- to 21-day-old female rat, the injections being given twice a day for 3 days, 1 cc per injection. On the morning of the fifth day (96 hours from the first injection) the rats are sacrificed and the ovaries examined for the appearance of grossly visible discrete corpora lutea. The anterior pituitarylike hormone of the serum being tested is considered normal provided none of the test animals or only the animal receiving the extract of 10 cc (test for 100 R.U. per 100 cc) gives a positive result. If all the animals show discrete corpora, the serum may be said to contain more than 333 RU of anterior pituitarylike hormone per 100 cc., a definitely elevated level. If the animal receiving the extract of 1.0 cc. and the 2 animals receiving the extract of 0.5 cc. are positive, whereas the fourth animal has no corpora lutea, the serum may be said to contain 200 R.U. of anterior pituitarylike hormone per 100 cc., an amount exceeding normal. For clinical purposes only 4 such tests are required with any 1 serum, unless the test for 333 R.U. per 100 cc. is negative and the 2 tests for 200 R.U. per 100 cc. fail to give check results. In this event the test for 200 R.U. per 100 cc. is repeated on 2 more immature rats, and if more than 1 of the 4 animals receiving an extract of 0.5 cc. show definite corpora, the anterior pituitarylike hormone may be considered to exceed normal levels.

Inasmuch as the reading of the end point requires considerable experience and even then is not always clear-cut, the importance of making check determinations with further specimens from the same patient and of using a series of at least 4 tests for each serum cannot be overemphasized. No patient should be reported as having excessive anterior pituitarylike hormone unless high values are acquired in at least 2 specimens of serum.

In addition to excessive amounts of anterior pituitarylike hormone in the circulating blood in patients with pre-eclampsia the authors have also noted a decrease of progestin and "total" estrogen at a time when they normally increase, and a striking change in the metabolism of estrogens due to reduced progestin, this last abnormality being demonstrable at the time of the onset of clinically recognizable toxemia.

The exact significance of these changes is, of course, as yet entirely theoretical

Remote Prognosis of the Toxemias of Pregnancy—A large percentage of patients who have eclampsia will develop and maintain a residual hypertension, and a considerable but smaller percentage will have persistent albuminuria. Recently F. J. Browne and G H. Dodds³⁷ reported follow-up studies varying from several months to 12 years of 400 preeclamptic, eclamptic, hypertensive, chronic nephritic, and recurrently toxenic patients. Among the eclamptic and the preeclamptic patients in this group, hypertension was a residual lesion in 60.8 per cent and 50.9 per cent respectively. Not 1 case was found, however, of chronic glomerular nephritis resulting from eclampsia or preeclamptic toxemia

Patients who have had eclamptic toxemias are likely to have toxemia again if they become pregnant. Therefore, these women should be kept under observation after delivery longer than the usual period. They should not become pregnant again until at least a year has elapsed after childbirth and then only after careful examination indicates that they may stand the strain of another pregnancy.

PREMARITAL EXAMINATIONS

W. M. Brunet and J B Salberg's discuss the observations in 913 women patients receiving a premarital physical examination and necessary laboratory tests. The average age for the group of 913 women was 23 years, with a range from 16 to 57 years. The details of the sexual life, pregnancies, and abortions of the group are discussed Of the 913 women, 6 white and 3 negro women had received treatment for gonorrhea white patient had been treated for syphi-The number of applicants for marriage certificates in Illinois who have given positive blood Wassermann and Kahn tests amounts to 2 per cent The State health department reported 896 positive reactions out of 47,781 examined up to July, 1938, which is a rate of 1.9 per cent. Of the 913 women, 905 of whom were white, 7 white patients were found to have gonorrhea and 7 syphilis. None of these patients had both infections Of the 8 negroes, 1 was found to have latent syphilis and 2 were suffering from both gonorrhea and syphilis. The rate for the entire group is 2 per cent and for the white women alone, 1.5 per cent

The authors state that this law prohibiting the marriage of individuals with positive serologic tests is wholly unjust, and in persons with congenital syphilis it may be a violation of their constitutional rights. They seriously question the authority and legality of such a statute to prevent the marriage of individuals on this basis. The law should be amended so that the examining physician will be the final authority as to the physical fitness of persons desiring to marry

PUERPERIUM

Afterpains

Treatment—The treatment of afterpains and painful engorgement in the puerperium with testosterone propionate is reported by A. R. Abarbanel 39 Briefly stated, the therapeutic rationale for the use of testosterone propionate is as follows. All the sexual hormones are definitely bisexual in their action, though to a varying degree Embryologically, as well as biologically, the female gonad exhibits strong bisexual potentialities Normal human females excrete from onesixth to as much androgenic substances in their urine as do normal men Testosterone is not only strongly androgenic, but it is also a very potent gynecogen, especially as regards its stimulative action on the female genital tract. action is dual, however, in that it resem-

bles estrogens in many respects, yet on the other hand it may stimulate the action of progesterone.

Testosterone will inhibit rhythmic, intermittent contractility of the uterus as well as desensitize it to the action of pituitrin. The exact action of testosterone on the human breast is not yet known. Therefore, its use in mastalgias is purely empirical

Testosterone proprionate in a dose of 10 mg. subcutaneously, given within 2 hours postpartum, prevented afterpains, adequate relief was obtained in 82 per cent with a total of 10 mg. of testosterone divided between the intramuscular and subcutaneous routes.

In 50 patients with severe painful engorgement, it was found that 10 mg. of testosterone proprionate (5 mg. intramuscularly and 5 mg subcutaneously an hour later) gave practically complete relief in 92 per cent of the cases. No inhibition of lactation was noted in those mothers who continued to nurse their babies.

Puerperal Infections Due to Clostridium Welchii

Cl welchu, known commonly also as Bacillus aerogenes capsulatus and the gas bacillus, is a rather short gram-positive rod, nonmotile and growing under fairly strict anaerobic conditions. It forms capsules in the animal body and under certain conditions readily sporulates. The organism is found in soil, water, milk, dust, sewage, and the intestinal canal of man and animals.

The symptoms found in puerperal infection due to this organism are those of an exceedingly acute and fulnimating infection. Severe abdominal pain, vomiting and chills are invariably present. The temperature is usually elevated, there is marked tachycardia and prostration is extreme, with hypotension. It is charac-

teristic that patients dying with this infection are usually mentally clear up to the time of death. Jaundice and a deep mahogany cyanosis due to destruction of the red blood cells by hemolysins are occasionally seen and may develop with great rapidity. The mortality is then practically 100 per cent. It is important to note that evidence of gas formation in the tissues, which is so commonly seen in surgical conditions, is found infrequently in obstetric infections due to this organism, even up to the time of death.

Puerperal infection with *Cl. welchii* is commoner in postabortal conditions than in puerperal infections following the birth of a viable child.

J. F. Sadusk, Jr., and C. P. Manahan⁴⁰ report the treatment with *sulfa-nilamide* of 2 severe postabortal infections due to *Cl welchii*, both with positive blood cultures.

The early diagnosis and immediate therapy of gas bacillus infections is important in view of the fulminating character of these infections

In cases of severe infection, with signs of marked toxicity, in which an early diagnosis has not been made, it would seem logical to administer both sulfanilamide and specific antiserum in massive doses, the latter for the purpose of neutralizing the toxins formed and the former in order to control the local lesion and the bacteremia. Sulfanilamide should be given in massive doses during the stage of bacteremia, at least $1\frac{1}{2}$ to 2 drams (6 to 8 Gm.) a day, divided into equal doses given every 4 hours throughout the 24-hour period. The concentration of sulfanılamıde in the blood should be followed daily, and the usual precautions should be taken to determine the onset of toxic reactions as early as possible. It is wise to administer sodium bicarbonate orally, in doses of from 1

to 2 drams (4 to 8 Gm.) a day, in order to prevent the development of acidosis.

Severe Puerperal Infection

Treatment—Large doses of sulfanilamide were given by C. A Gordon and A. Rosenthal⁴¹ to 118 patients with severe puerperal infections of the genital tract, regardless of their etiology. Clinical response was prompt and satisfactory in 45 cases, or 38 per cent. In an additional 45 cases, or 38 per cent, results were not convincing, yet good enough to make these investigators feel that the drug may have played an important part in recovery. In 23 cases, or 20 per cent, no beneficial results were observed. There were 5 deaths, a mortality of 4 per cent.

Administration is definitely associated with toxic manifestations, none of which need to be a serious hazard Usually obvious and rarely severe enough to warrant discontinuance of therapy, toxicity is actually low A moderate fall in hemoglobin is common and harmless. authors have seen no case of agranulocytosis. Acute hemolytic anemia cannot be foreseen or prevented since it is apparently due to idiosyncrasy, developing quickly within the first few days of treatment after comparatively small doses of the drug Rapid drop in hemoglobin and erythrocytes, leukocytosis, marked reticulocytosis, bilirubinemia, and urobilinuria are noted Daily blood counts for at least the first 5 days are essential. Though it occurs but seldom, and transfusion is effective, it is because of the ever present danger of serious blood changes that indiscriminate administration of sulfanilamide is inadvisable. Other toxic manifestations are readily observed clinically and subside when the drug is withdrawn.

In mild cases of puerperal infection, sulfanilamide is not indicated. Certainly proper bacteriological investigation should precede therapy, but it is not essential. Intrapartum infections should be treated with sulfanilamide at once. Report on Streptococcus hemolyticus may be had in 24 hours; vaginal swab culture is better than intrauterine. If hemolytic streptococci are found, drug therapy should be discontinued only under exceptional circumstances, and one should not be too quick to stop its administration because bacteria have disappeared or a diagnosis of drug fever has been made.

Experience indicates that optimum benefit may be expected with spaced maintenance doses of 20 to 30 grains of sulfanilamide and moderate fluid restriction, provided a large initial dose has been given the patient

In severe puerperal infections of the genital tract whatever their etiology, sulfanilamide may be used and should be, provided the patient is in a hospital where its administration may be controlled

Vaccination for Puerperal Infections—A second series of 177 pregnant women vaccinated against puerperal infections is the subject of the report by J B Bernstine and G. W Bland 42 The vaccine consists of 5 strains of Streptococcus hemolyticus, 8 of Streptococcus viridans, 2 of Staphylococcus aureus, 2 of Bacillus coli communis, 4 of Streptococcus nonhemolyticus, and 10 of Staphylococcus albus. The respective percentages of these strains in the vaccine are 35, 15, 15, 15, 10 and 10

The patients (228) in both series were delivered with no fatalities. The puerperal morbidity was 5.4 per cent as compared to the morbidity of the nonvaccinated women, which was 19.2 per cent. Ninety male and 82 female children were born to the 177 vaccinated patients. There were 3 abortions and 2 stillbirths. In the entire group there were 3 abnormalities—hemangioma of the maxilla,

supernumerary digits and left clubfoot. The vaccine was administered to pregnant women with various complications in addition to their pregnant state. These complications varied in type and severity, and yet not a single case was observed that presented an aggravation of the preexisting condition. The patients were not hand picked but represent a cross section of the average obstetric practice with its associated complications.

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ORTHOPEDICS

By JOHN R. MOORE, M.D., and JESSE T. NICHOLSON, M.D.

BACKACHE

Spondylolisthesis as an Etiologic Factor—Meyerding¹ reviewed a series of 583 cases of spondylolisthesis seen at the Mayo Clinic. Ten per cent of the patients had no complaints and the

recognition was incidental to examination for other conditions Eighty per cent complained of backache Seventeen per cent had radiation of pain in sacroiliac, hips or legs Less than 2 per cent complained of any deformity, stiffness

or paralysis. The diagnosis was generally made following inspection and palpation. A forward and downward displacement of the lumbar spine on the sacrum gave a prominent spinous process of the latter. The erecti spinae muscles were prominent. The torso appeared shortened and the pelvis broad.

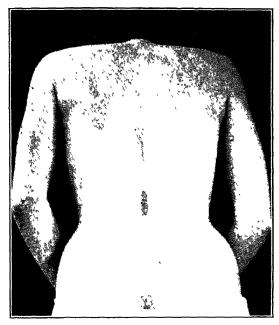


Fig 1—Typical deformity of spondylolisthesis, showing depression, and forward and downward displacement of lumbar spine. (Meyerding J Λ M Λ)

Frequently an abdominal crease was found. Subjects with extreme spondylolisthesis had a list or waddle when they walked. The ribs appeared to telescope within the pelvis. The roentgenogram in the antero-posterior view showed a shortened lumbar spine with superimposed fifth lumbar vertebra on the sacrum, cocked-up spinous processes, separation of the neural arch and a spina The lateral roentgenogram bifida showed an anterior luxation of the body of the vertebra. On the basis of this film the said luxation was graded, 1, 2, 3 or 4, according to whether the posterior border of the slipped vertebra was on the first or fourth quarter of the body below. Seventy per cent of the cases were individuals of laborious occupations. It was believed that had they pursued less strenuous activities in life they would not have developed symptoms Fifty per cent of the cases developed symptoms between 30 and 40 years. Trauma was an etiological factor in symptoms in but 48 cases. No relationship between the degree of luxation and trauma could be established. In 82 per cent the deformity occurred at the level of the fifth lumbar vertebra and the sacrum In but 10 per cent was the deformity graded 3 and 4. A displacement of the deformity backward instead of forward occurred in but 4 per cent

Treatment—If trauma was the recognized cause of the spondylolisthesis an immediate attempt should be made to reduce the deformity. The patient

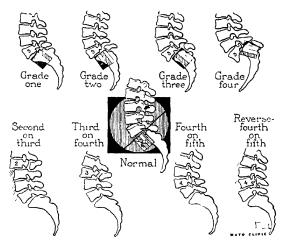


Fig 2—Four grades of spondylohisthesis (Meyerding J A, M A)

was placed recumbent, the legs were elevated to right angles to the thighs and the thighs to right angles to the spine Kirschner wire was inserted through the lower end of the femur to maintain this position by means of overhead traction

After 6 weeks a double hip spica was applied with the legs in extension. At the end of 3 months the patient was allowed to be up and walk with a back brace. If there was a recurrence of the subluxation, the spine was fixed with bone graft.

Eighty-three per cent of the cases were treated with supportive corsets. Sub-

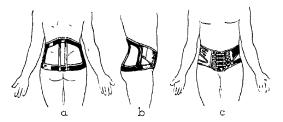


Fig 3—Rocking-chair type of back support made of steel and leather (Meyerding J A M A)

jects who continued to follow laborious occupations all were subject to repeated strain and required an operation. Surgical fixation of the joints was accomplished by using a graft of bone from the tibia, placing same in a prepared bed of cancellous bone overlying the sacrum and laminae on either side of the spinous processes as far as the third lumbar vertebra

BICEPS BRACHII

Acute Traumatic Dislocation of the Tendon of the Long Head—Six cases of dislocation of the biceps tendon resulting from injury were reported by Abbott and Saunders ² In all the cases the injury was followed by pain and swelling of the anterior aspect of the joint and there was complete disability of the affected shoulder. The patient complained of pain with weakness and limitation of motion in forward flexion and abduction of the shoulder and pain

on forced supination of the forearm against resistance with the elbow held in flexion. The principal findings were swelling over the anterior aspect of the shoulder, tenderness, more pronounced over the bicipital groove, and a definite snapping sensation on abduction and external rotation of the shoulder all the cases there appeared at operation a displacement of the tendon over the lesser tuberosity. The best approach is obtained by the anterior muscle splitting incision by Codman Local anesthesia and the sitting position greatly facilitate the operation In uncomplicated cases of dislocation the result is best obtained by fixation of the tendon in bicipital groove When other lesions occur simultaneously an adequate result may be obtained by replacement of the tendon and repair by fascia of the roof to its groove

BONE AND JOINT SYPHILIS

Jostes and Roche³ reviewed 111 clinically active bone and joint lesions resulting from syphilitic infection.

In congenital syphilis, osteochondritis and epiphysitis were the most characteristic, but periositis, osteitis, osteochondritis, and osteomyelitis occurred in the order presented. Synovitis and dactylitis were less frequently encountered

In the acquired syphilis, periostitis, osteitis, osteomyelitis and Charcot's joints resulted

The treatment was constitutional and anti-syphilitic. Surgery was rarely of value in Charcot's joints and should not be undertaken until the patient is well under the influence of anti-syphilitic treatment which included the administration of courses of arsphenamine and the heavy metals.

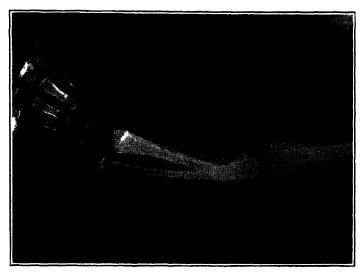


Fig 4—Osteochondritis Congenital syphilis Involved areas of distal ends of radius and ulna quite obvious (Jostes and Roche $\,$ J $\,$ Missouri $\,$ M $\,$ A $\,$)

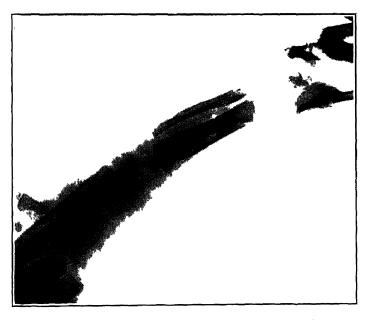


Fig 5—Periostitis of long bones Congenital syphilis (Jostes and Roche J Missouri M A)



Fig. 6—A, B, Osteitis (gummata of skull) Congenital syphilis C, Active ostcomyclitis of tibia D, Healed (Jostes and Roche J Missouri M A)

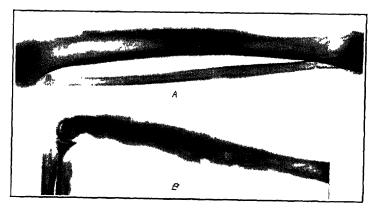


Fig 7—A, Periostitis (saber shin) Late congenital syphilis B, Osteomyelitis of the humerus Acquired syphilis (Jostes and Roche J Missouri M A)

ORTHOPEDICS



Fig 8—Charcot joint Ankle Acquired syphilis. (Jostes and Roche J Missouri M A)



lug 9--Charcot hip, right. Old subtrochanteric transverse fracture with extensive calcule overgrowth on left. Acquired syphilis. (Jostes and Roche. J. Missouri M. A.)

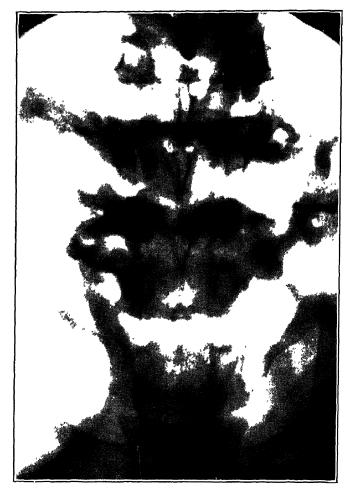


Fig. 10—Charcot joint lumbar spine. Massive destruction of lumbar vertebra with loose bodies on either side. Acquired syphilis. (Jostes and Roche. J. Missouri M. A.)

BONE REPAIR

Influence of Vitamin D—Compere, Hamilton and Dewar, using 4 groups of rats, tried to determine the effect of vitamin D on bone repair. In the first group, which had sufficient vitamin deficiency to produce active rickets, delayed and nonumon was encountered. In the second group of rachitic rats which were given sufficient vitamin D, the rickets healed and more rapid repair and better quality of healing of the fractures occurred. In the third group, growing rats kept constantly on vitamin D and phosphorous deficiency diet, their bones were shorter and more fragile than

those in the other groups. The fourth group of rats, kept on a well-balanced diet with no vitamin D supplement, were twice as large as those in the other 3 groups Their bones were proportionately stronger. The healing was more rapid and the function was restored more It was concluded that suppromptly plementary doses of vitamin D were only indicated in the care of fractures if there was a demonstrable vitamin D deficiency Prolonged use of large doses of vitamin D not only delayed healing of fractures but produced degenerative changes in the bones of the experimental animals.

BONE TUMORS

Sarcoma

Simmons⁵ reported the results of 47 subjects with primary malignant tumors of long bones, excepting plasma cell myeloma, treated at the Massachusetts General Hospital from 1920 to 1932. His conclusions from this series were as follows:

"1. The prognosis in a series of consecutive cases of osteogenic sarcoma is not as poor as

- "6. Of 7 cases in which amputation was done and in which cartilage was the predominating tissue, 5 patients are well (70 per cent).
- "7. Of 16 cases in which amputation was done and which may be placed in an anaplastic group, 1 is well (55 per cent).
- "8. Two cases of reticulum cell sarcoma in which amputation was done are reported. One patient is well 14 years later, and 1 died 12 years later of a tumor of another bone, the character of which was not determined.
- "9. Of 8 cases of Ewing's sarcoma, 4 patients were treated surgically and 4 by radiation. All patients died of the disease"

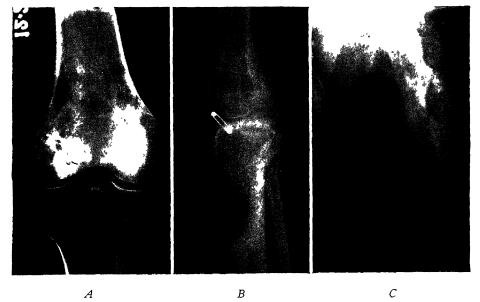


Fig. 11—.1, Roentgenogram of femur. B, Roentgenogram of tibia. C, Roentgenogram of humerus. (Parker and Jackson. Surg., Gynec. & Obst.)

is generally believed if the tumors are removed by radical surgery

- "2 ()f 28 cases of osteogenic sarcoma in which amputation was done, 11 patients, 39 per cent, are living without disease 5 or more years after operation
- "3. The prognosis depends more on the amount of differentiation of the cells comprising the major portion of the tumor than on any 1 other factor
- "4 If the tumor is composed in large part of adult fibrous tissue or cartilage, the prognosis is better than it the cells show marked anaplasia.
- "5 In 5 cases in which fibrous tissue predominated, patients were treated by amputation All are well (100 per cent).

Primary Reticulum Cell Sarcoma—

Parker and Jackson⁶ claimed that prior to 1931 primary reticulum cell sarcoma was variously classified as Ewing's sarcoma, Hodgkin's disease, lymphosarcoma, or chronic inflammation. It differed from the generalized reticulum cell sarcoma, which was a disease of middle and old age, in that it occurred most frequently in long and flat bones, rather than skull and vertebrae. The chinical onset generally was attributable to trauma. The chief symptom was pain at site of lesion or referred to a neigh-

boring joint. This pain was not relieved by rest. In but 8 of the 17 cases reported was any enlargement of the involved part observed. The general health and blood chemistry were not affected. The tumor cells were identical with reticulum cell sarcoma of lymph nodes tled destruction in the medullary cavity. In the advanced lesions marked destruction with little regeneration was apparent.

Treatment—Diagnosis was made by biopsy. Immediate amputation and radiation were followed by the greatest

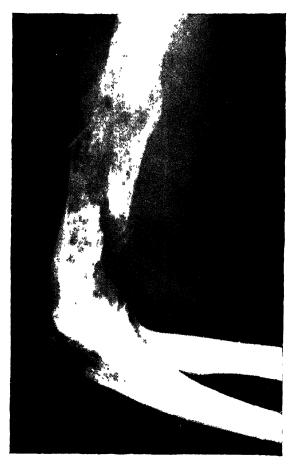


Fig. 12—Roentgenogram of humerus. (Parker and Jackson. Surg., Gynec & Obst.)

and other tissues. Grossly the tumor was firm, smooth and glistening pinkish gray with areas of necrosis merging into cavities. There was frequently invasion of the surrounding muscle. The roentgen appearance was not particularly pathognomonic. The lesion occurred frequently in the metaphysis and extended into the diaphysis. There was greater bone destruction than formation, except when complicated by a pathological fracture. Early there was a mot-

number of survivors from 6 months to 14 years from onset

Bone Necrosis, Aseptic

Infarction of Bones in Caisson Disease—Four cases of Caisson disease with extensive changes in the skeleton were studied clinically and roentgenologically. Lesions were revealed in the diaphysis and epiphysis of certain bones with corresponding joint changes. There was no assurance as to whether the necrosis



Fig. 13—Case 1 Deforming arthritis of both hips and loose body, a (Kahlstrom, Burton and Phemister. Surg, Gynec & Obst)

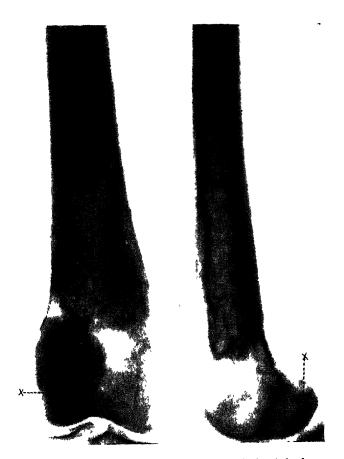


Fig. 14—Case 1. Central necrotic area in the shaft of the left femur. The calcified and ossified zone of demarkation and the calcified necrotic island in the external condyle, 1, are clearly shown. (Kahlstiom, Burton and Phemister. Surg., Gynec & Obst.)

was produced by embolism of the end arteries through nitrogen gas or by obstruction of the blood vessels through liberation of the nitrogen from other tissues This latter theory was based on the fact that the long bones were rich in fatty



Fig 15—Case 1 Loose bodies in shoulder joint and walled-off necrotic area in upper half of humerus (Kahlstrom, Burton and Phemister Surg, Gynec and Obst.)

marrow and that fat absorbed relatively large amounts of nitrogen, the change in pressure liberated the gas, causing direct pressure on the vessels and other tissues within the bones. This was further substantiated since the long bones were the only ones involved. Contradictory, however, was the involvement of the diaphysis without the involvement of the epiphysis and the involvement of the epiphysis, especially of the head of the femur, without the diaphysis. Experimentally the changes could not be

produced through air embolism of the lower limbs of dogs.

BURSITIS

Subcutaneous Dorsal Digital Bursitis—Directly beneath the skin overlying the digital articulations were found fairly constantly small bursa ⁸ Following a cut, scratch or an abrasion of the dorsum of one of the finger joints a swelling, redness and tenderness of the joint occurred some days after healing had taken place. The tenderness was characteristic as it was only on the dorsum of the joint and pain was present only on flexion of the



Fig 16—Acute dorsal digital subcutaneous bursitis over distal joint of fifth finger. The bursa was uniooted with a sharp scalpel 5 days before photograph. The exposed bursa appears as the central depressed area, its walls no longer sharp and steep and healing underway (Howard, Surgery).

finger The wound might reopen or the bursa rupture and drain beside the healed scar. This gave relief of symptoms until healing again took place. If the condition was recognized early the wound edges were kept apart and healing permitted by secondary intention. In the chronic cases it was necessary to take a scalpel and remove the roof of the bursa, just leaving the floor and shallow walls exposed Cases recognized early averaged 13 4 days of treatment. Those in which a 74-day average interval had elapsed before the bursitis was recognized, resulted in an average care of 92 days.

COMPOUND FRACTURES

Local Implantation of Sulfanilamide—Thirty-nine compound fractures and 2 cases of compound dislocations were treated as follows by Jensen, *et al* ⁹

- 1 Thorough débridement.
- 2 Implantation of 5 to 15 Gm crystalline *sulfanilamide*.
- 3 Primary closure of the skin avoiding tension.
 - 4 Complete reduction of fracture.
 - 5. Complete fixation.
- 6 Systemic care—medication, sedation, transfusion, etc

Results—In the 39 compound fractures and 2 compound dislocations treated in the above manner primary healing of the wound occurred in every instance

Experimental Work—Guinea pigs were used as the experimental animal, compound fractures of the ribs were produced by surgical procedure, *Staphylococcus aureus hemolyticus* was introduced into the wound. In 10 animals in which 7½ grains (0.5 Gm.) of crystalline sulfanilamide were placed in the wound before closure, 7 healed in a perfectly normal manner. In 7 control animals, 5 developed severe wound infection with osteomyelitis of the rib, 2 healed without suppuration.

In 94 m which sulfamilamide was not applied locally or systemically, 75 per

cent infection occurred. There were 7 cases of gas gangrene.

Introduction of sulfanilamide locally as a means of sterilization of compound wounds would seem to be a rational procedure.

CONGENITAL DEFORMITIES

Preliminary observations of the embryology of the hip joint were presented by D A De Santo and P. C. Colonna.¹⁰ This was done by means of horizontal serial sections through the embryo or fetus, the embryos being 6, 10, 14, 20, 25, and 30 weeks old.

Fig. 17 shows a sagittal section of a 6-week embryo. The cartilages of the ilium and femur are formless structures, and only a suggestion of the joint space exists

"In the 10-week embryo the iliac cartilage is well formed, as is the acetabular cavity. The cotyloid ligament and the ligamentum teres are present but no definite capsule is developed, and there is no vascularization of the cartilaginous structures."

Fig 19 shows a 14-week fetus "The shape of the femoral head and that of the acetabulum more closely resemble the shape of these structures in the infant. The cartilages show beginning vascularization although the capsule still remains unidentified"

"In the 20-week fetus the acetabulum begins to ossify, and ossification proceeds rapidly throughout the remainder of intrauterine life. The capsule is present and is vascular. The blood supply of the femoral head and neck of the trochanter may in part be traced to blood vessels entering by way of the capsule. The trochanter receives an additional blood supply from the lateral muscles. The ligamentum teres can be noted, and

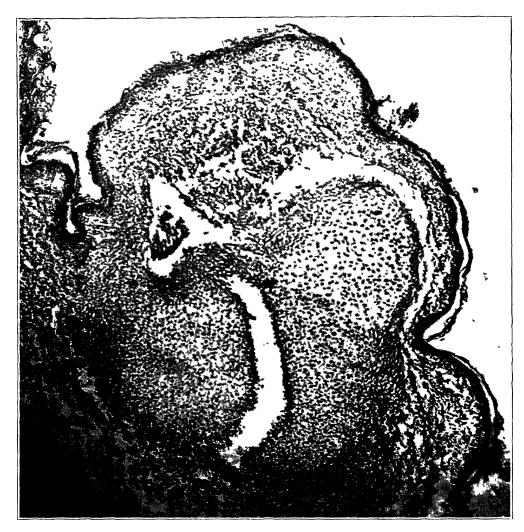


Fig. 17—Sagittal section of a 6-week embryo, showing the primitive hip joint. The acetabulum is to the right. (De Santo and Colonna. Arch. Surg.)

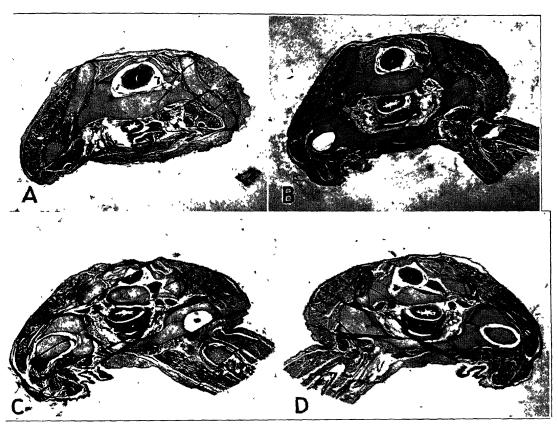


Fig. 18—A, Horizontal section through a 10-week embryo at the level of the sacrollac joint. The iliac cartilage is undergoing ossification. The dorsal laminas are not fused. B, Same embryo. The section shows the acetabulum on the left side at the level of the pubic symphysis anteriorly. Notice the well-formed cotyloid ligaments and the absence of any blood supply to the cartilages C, Same embryo. The head of the temus is flattened and club shaped. The ligamentum teres is avascular. Notice the absence of a joint capsule. D, Same embryo. The general features are the same. The blood supply of the head is more marked from the capsular side. The cotyloid ligaments are present. (De Santo and Colonna. Arch. Surg.)

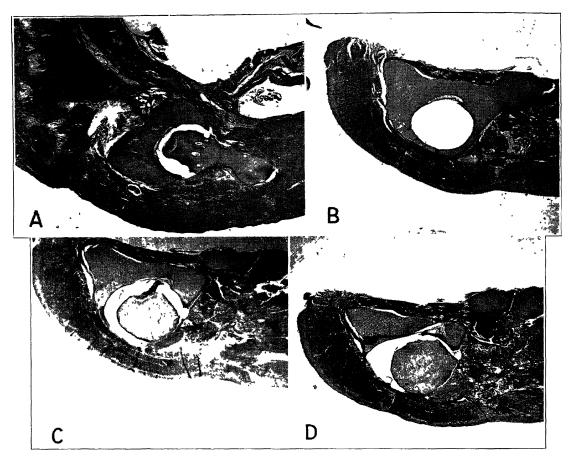


Fig 19—A, Sagittal section through the hip joint of a 14-week fetus, showing the acetabulum and the ilium. Notice the blood supply of the intertrochanteric region. B, Same fetus in horizontal section, showing the acetabulum and a portion of the pubic ramus. There is beginning vascularization of the acetabulum at the site of attachment of the ligamentum teres. C, Same fetus, showing the head of the femur in the acetabulum. The ligamentum teres is readily seen. It has a slight blood supply, which is not apparent in this magnification. The joint capsule is still not formed. D, Same fetus. Note the separate iliac and pubic components of the acetabulum. (De Santo and Colonna: Arch. Surg.)

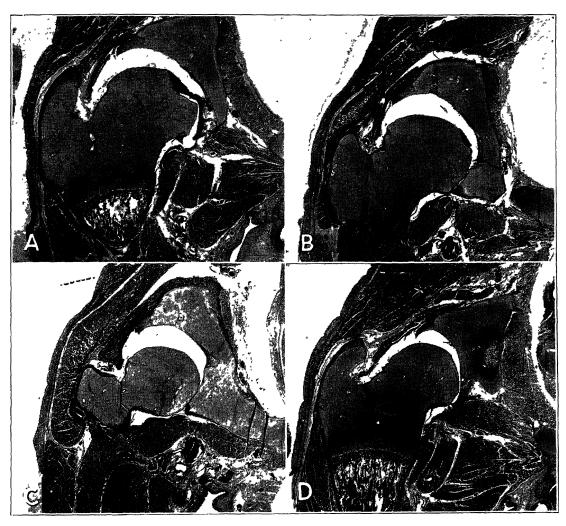


Fig 20—A, 20-week fetus, showing the head, neck and trochanter of the femur and the acetabulum. Notice the profuse blood supply of all the cartilages. The ligamentum teres is seen and also contains a profuse blood supply. The capsule may be seen for the first time, inserting into the notch between the neck and the trochanter. There is a vascular membrane covering the surface of the upper end of the neck, this represents the primitive synovium, not readily seen in the low magnification. B, Same fetus, showing the same complete acetabulum. C, Same fetus. Notice that the hip joint is at the level of the pubic symphysis. D, Same fetus, showing the center of ossification in the acetabulum. (De Santo and Colonna. Arch. Surg.)

the synovium appears in the acetabulum and around the neck of the femur. It becomes increasingly vascular in the older fetuses."

Fig. 21 shows a fetus of 30 weeks. Little difference is seen in this fetus and that of the 20-week one.

or all of an extremity. There was no pitting edema. It was divided into 2 types, the simple and familial (Milroy's disease) which were indistinguishable clinically. Roentgen study offered considerable aid in differentiating this condition from other clinical conditions. The



Fig 21—Fetus of 30 weeks. There are no striking changes from the appearance described for the 20-week fetus, but the structures are larger. The center of ossification in the acetabulum is somewhat larger. Some of the head is missing. (De Santo and Colonna: Arch. Surg.)

CONGENITAL ENLARGEMENT OF THE EXTREMITIES

Cooperstock¹¹ stated there are chiefly 3 types of congenital enlargement, lymphedema, hemangiectatic hypertrophy and Recklinghausen's neurofibromatosis. These conditions were not to be confused with congenital hemihypertrophy in which overgrowth involved 1 entire side of the body or the congenital hypertrophy of parts of an extremity, such as fingers or toes (macrodactylia).

Congenital lymphedema (lymphangiectasis) was present at birth, restricted to the skin and subcutaneous tissues or part

x-ray films showed hypertrophy of the tissues peripheral to the muscle. In ordinary edema all the tissues of the extremity were involved in the thickening. In chronic inflammatory processes the skin and muscular aponeurosis appeared thickened and there was an extensive network of fibrous trabeculation in the subcutaneous tissues between them. The trabeculations of the subcutaneous tissue had been observed in 2 instances of uncomplicated Milroy's disease.

Congenital hemangiectatic hypertroplay of extremities was due to an increase of vascularity, either dilatation of veins or both arteries and veins, or the capil-

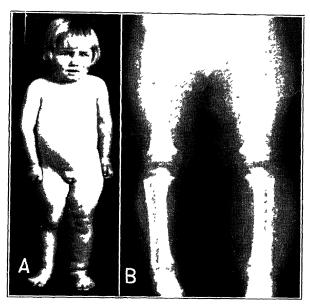


Fig. 22—4, A 3-year-old patient with nonfamilial congenital lymphedema (lymphangiectasis) B, Roentgenogram showing lymphedema of the subcutaneous tissues of the left leg. (Cooperstock Am. J. Dis. Child.)

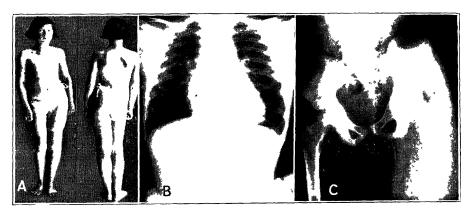


Fig. 23—A illustrates marked overgrowth of the left leg associated with congenital arteriovenous fistula, B, cardiac enlargement, and C, marked increase in the size of left femur and hypertrophy of the soft tissue structures. (Cooperstock Am. J. Dis. Child.)

lary bed which occurred with extensive vascular nevi. Congenital vascular anomalies with arterial anastomoses frequently were contributing cause.

Recklinghausen's neurofibromatosis mostly involved the regions of the head, trunk and extremities resulting from development of large molluscum fibrosum (involvement limited to the skin) or to plexiform neurofibroma (lesion confined

embryonic form of cartilage which was disc-shaped In some instances the form of the disc had not been completely preserved but was substituted by a membranous connection filling the defect There was generally no associated trauma. It was the external cartilage Sudden attacks of pain occurred when the knee was flexed or extended due to the catch of the cartilage. This was fol-

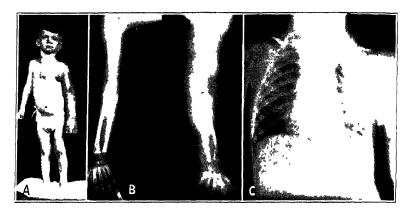


Fig. 24—A, A 3-year-old patient. Recklinghausen's neurofibromatosis has produced marked enlargement of the left arm. Neurofibromatous swelling on the left side of the neck and distortion of the anterior wall of the chest are seen. B shows that the long bones of the left arm are longer but more slender than those of the opposite side, there is overgrowth of the soft tissue structures of the left arm and hand. Creveals a mediastinal mass, probably neurofibromatous. (Cooperstock Surg., Gynec & Obst.)

to the distribution of nerve or nerve plexus) There was generally pigmentation of overlying skin. Associated disturbances of bone growth consisted primarily of increased length and thickness of long bones with irregularity in shaft outline. These occasionally were large tumors projecting from the cortical structures imbedded in cystlike cavities. Pathologically they consisted of neurofibromous tissue. Shortening of the extremity occasionally resulted when a neurofibromous growth involved an epiphysis.

DISCOID CARTILAGE— TRIGGER KNEE

Ober¹² described the discoid cartilage in the knee as due to a persistence of

lowed by a limp and some swelling. As growth continued the cartilages became thickened in the peripheral portion so that they projected from between the condyles of the femur and tibia. The thickened portion became caught between the articular surfaces. In these areas cystic degeneration was common. Examination might show atrophy of the calf and thigh muscles and some increase in joint fluid. The joint was occasionally locked in flexion but rarely in extension. On palpation of the extended joint, a small tumorlike mass was felt over the lateral aspect which disappeared on flexion and reappeared on extension with a definite snap or jerking sensation. The treatment was the removal of the cartilage.

ELBOW

Madelung's Deformity and Associated Deformity

Thompson and Kalayjian¹³ described Madelung's deformity of the wrist as a curvature in the distal half of the radius in the antero-median direction with a prominence of the distal end of the ulna dorsally and a palmar luxation of the wrist with ulnar deviation of the hand.

The roentgen film revealed distraction atrophy on the radial head. Its typical onset was in early adolescence. It was due to a premature closure of the distal radial epiphysis and not to the usually ascribed causes as fracture or traumatic separation of the epiphysis, congenital dislocation, infection of the radial epiphysis, arthritis, rickets and osteochondritis. The symptoms were pain and limitation of motion of the wrist.



Fig. 25—Case 1. Deformity in right wrist as compared to the left at age of 13 years and 3 months. (Thompson and Kalayjian. Surg., Gynec & Obst.)

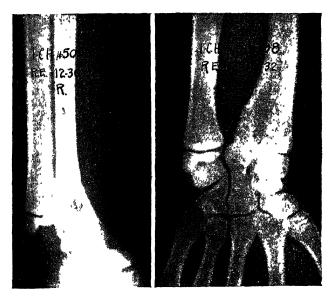


Fig 26—(ase 1 Right wrist showing involvement of radius, separation and dorsal displacement of ulna, and wedging of carpals, at 12 years and 10 months. (Thompson and Kalayjian Surg., Gynec. & Obst.)

The treatment advocated was resection of a portion of the diaphysis of the ulna to relieve pain and, after growth was complete, corrective osteotomies at points of greatest curvature in both bones to reduce the deformity.

State I, the early slipping stage, required discontinuance of weight bearing, by means of crutches, elevated shoe on good leg and caliper brace of affected side. State II, a gradual slipping in which the epiphysis was still unseparated or

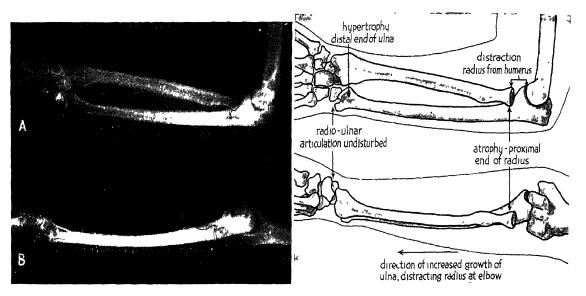


Fig. 27—Case 2. a, Left. Retouched roentgenogram to illustrate changes at elbow, i v, atrophy and distraction of head of radius, and hypertrophy of capitellum. b, Diagrammatic representation of Fig. 27, a. (Thompson and Kalayjian. Surg., Gynec. and Obst.)

FEMUR

Femoral Epiphysis

Slipped Femoral Epiphysis

thormley and Fairchild¹⁴ stressed trauma as the etiological factor in production of slipped femoral epiphysis. The endocrine disturbance (Frohlich syndrome) which was observed in approximately 50 per cent of their cases was a factor only in that the increased weight of these individuals produced greater strain on the epiphysis

It was believed that slipping epiphysis occurred at adolescence due to an increase in the inclination of the epiphyseal line and rapid growth at that age.

Early and accurate diagnosis and careful observation were most important

The treatment depended upon the degree and duration of the separation.

in which the head of the femur lay loose, in the latter case gentle manipulation could be tried for reduction, otherwise, both were reduced by open operation to give a minimum amount of trauma to the head, and epiphysis. Stage III, a complete slip of long standing, was treated by open reduction and replacement of the head of the femur if the epiphysis was loose or an osteotomy through the neck to correct the external rotation and shortening of the leg if the epiphyseal line was closed. In adult life an acetabuloplasty or, if a painful hip, some form of arthrodesis are the best procedures

Internal Fixation of Trochanteric Fractures

It was pointed out by J. Albert Key¹⁵ that the mortality of 214 trochanteric fractures of the femur was 38 per cent.

The mortality of 166 intercapsular fractures in the same hospital was 259 per cent. They were not only more frequent, but the subjects were older. Through the use of the Smith-Petersen nail, the ability to get the intercapsular fractures up and about more quickly had definitely been in favor of their lowered mortality A series of 15 trochanteric fractures was fixed with a Smith-Petersen nail Each of the patients was over 80 years and but 2 died 6 months after the fixation of an intercurrent infection. success of this procedure depended definitely on certain principles. First, adequate reduction Second, that the cortex of the shaft be drilled through before the Smith-Petersen nail was inserted or else there would be a splintering of the cortex which would make fixation impossible Third, that the telescoping of the neck into the shaft be taken into account so that a nail of too great length would not be used, thus engaging in the acetabulum Fourth, the head of the nail could not be driven into the cortex of the shaft without splintering it and losing fixation. Fifth, the nail must engage well into the cancellous bone of the head and not just enter into the neck The period of bed rest depended largely upon the position of the fracture, the reduction and the relative fixation secured by the nail Care was taken to maintain the hip in abduction at all times and if the patient turned on the good side, pillows were placed under the fractured hip to hold it in abduction. In 2 to 4 weeks the patient was allowed to sit on the edge of the bed and dangle the legs or even helped into a chair, but the leg was lifted at all times. No weight bearing was permitted and even walking on crutches without weight bearing was discouraged until union was firm x-rays were taken at 2-week intervals

If there was any question of a slip, then traction of 10 to 15 lb. was applied to the extremity until the deformity was corrected and the fracture fairly well healed (The editors wish to stress the number of pitfalls there are in this method of treatment.)

Intracapsular Femoral Neck Nonunion

The methods reviewed by W R Hamsa¹⁶ are as follows:

- 1 The Albee bone graft
- 2. Smith-Petersen nailing.
- 3 Whitman reconstruction.
- 4. Albee reconstruction
- 5 Colonna reconstruction.
- 6 Magnuson reconstruction.
- 7 Brackett reconstruction
- 8 Lorenz osteotomy
- 9 Schanz osteotomy.

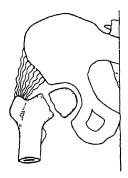
The treatment is decided upon according to the patient's general condition in a manner as follows:

- A If the patient's general condition is good
- I Living head—the author recommends open reduction and fixation with the Albee bone graft
- 2 Head necrotic and neck present—the author recommends the reconstruction by the Albee or Whitman method
- 3 Neck is absent—the author recommends the reconstruction by the Colonna method
- 4 Osteoarthritis is present—the author recommends the arthrodesis of the hip as the method of choice
 - B If the patient's general condition is fan
- 1 Head living—the author recommends the reconstruction by Brackett or Magnuson
- 2 Head necrotic—the Lorenz or Schanz osteotomy should be employed
 - C If the patient's general condition is poor
- 1 Head living or dead—the treatment is osteotomy by Lorenz or Schanz or simply some form of mechanical support

A total of 41 cases was treated and the results are as follows.

Type of Operation	Results
Albee bone graft, 5 cases	60% successful
Smith-Petersen nail, 2 cases	All failures
Whitman reconstruction, 18 cases	Good in 5, fair in 4, poor in 9
Brackett reconstruction, 3 cases	Good in 1, failure in 2
Lorenz osteotomy, 9 cases	Good in 2, fair in 2, poor in 5
Schanz osteotomy, 3 cases	Good in 1, fair in 2
Arthrodesis of the hip, 1 case	Good result

This article merits review because of the very excellent presentation of the many methods employed in nonunion of intracapsular fractures The illustrations are very clear The author's series is sufficient to justify his conclusions His experiences are similar to those in the majority of large orthopedic clinics



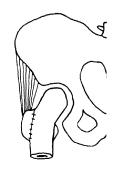
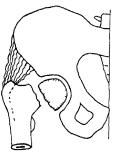


Fig 30—Whitman reconstruction (Hamsa. Surg, Gynec & Obst)



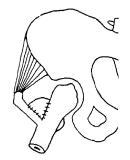


Fig. 31—Albee reconstruction (Hamsa Surg, Gynec & Obst)

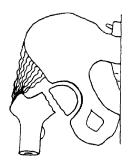


Fig 28-Albee bone graft (Hamsa Surg., Gynec & Obst)

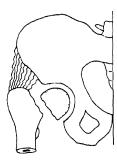
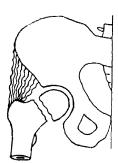




Fig. 32 - Colonna reconstruction (Hamsa Surg , Gynec & Obst)



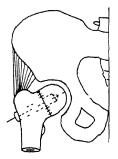
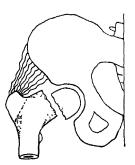


Fig. 29-Smith-Petersen nailing. (Hamsa Surg, Gynec & Obst)



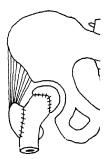


Fig 33-Magnuson reconstruction (Hamsa Surg, Gynec & Obst)

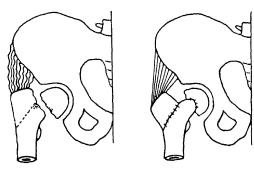


Fig 34—Biackett reconstruction. (Hamsa Surg, Gynec & Obst)

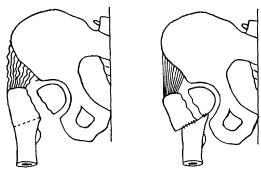


Fig 35-Lorenz osteotomy (Hamsa Suig, Gynec & Obst)

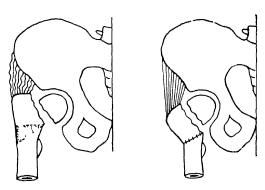


Fig. 36— Schanz osteotomy (Hamsa Surg , Gynec & Obst.)

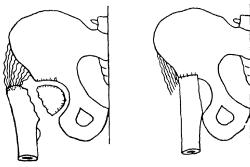


Fig 37— \text{\text{1throdesis of hip joint}} (Hamsa Suig, Gynec & Obst)

Obstetrical Fractures

Treatment—Arnold Pavlik¹⁷ reports on the work of Dr. Frejka. Dr. Frejka has discarded the treatment of obstetrical fractures of the femur by any method employing extension. Replacement of the fragments is best obtained by abduction of the limbs in a plaster-of-Paris bandage. The position is similar to that used in congenital dislocation of the hip. This position maintains axial alignment though it is usually accompanied by overriding. The shortening is compensated for during the healing process by overgrowth.

Figs 38-A and 38-B illustrate reduction and end result some 2 years afterwards

Comment—Four cases are illustrated in the article. No mention is made of the total number of cases treated by the method. It is difficult to draw conclusions referable to the general usefulness of such a procedure in view of the lack of sufficient data.

Pauwels' Reclination

A Physiological Reconstruction for Nonunited Fractures of the Neck-Karfiol¹⁸ reports 7 cases of nonunited intracapsular fractures of the neck of the femur treated by Pauwels' reclination The method described Pauwels in 1929 was based primarily on the fact that shearing and traction forces decidedly hindered the healing processes of the fractures of the neck of the femur, thus leading to nonunion. By means of the Schanz high subtrochanteric osteotomy Pauwels was able to change the mechanical forces by decreasing to less than 30° the angle of the fracture In 7 cases, reported by Karfiol, treated according to the above method, the results were as follows:

1. Physiological stimulation of callous formation occurred

- 2. Prevention of further displacement through the upward gliding of the shaft
- 3. Stability of the affected leg with safe bearing of weight
- 4. Reconditioning of the pelvitrochanteric muscles
- 5 Downward displacement of the greater trochanter.
- 6. Increased abduction of the injured leg, etc.

According to the author there is little pain after the operation. The period of hospitalization is from 10 to 11 weeks



Fig. 38— I, Case 2. Obstetrical fracture of the left femur in an infant 17 days old. There is displacement of the fragments in every direction, with considerable shortening of the femur and an irregularly developed bone callus. (Paylik: J. Bone & Joint Surg.)

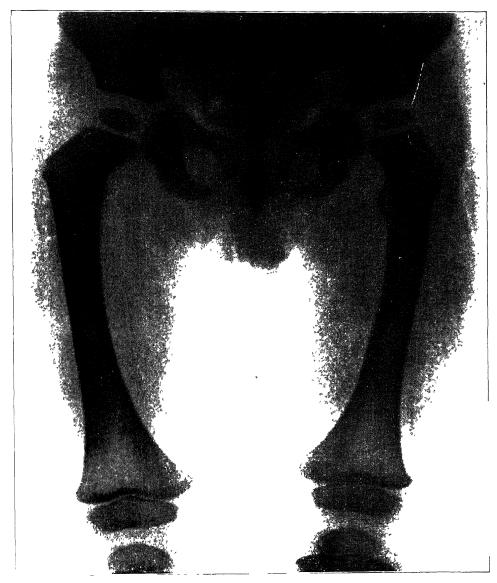


Fig. 38—B, Case 2. Rochtgenogram at the age of 27 months, showing complete consolidation of the fracture with slight obliquity of the neck of the left femur. The neck has united with the shaft at an angle of 160 degrees. The length of the right femur is 19.0 cm, and that of the left femur is 18.7 cm, making the left femur 0.3 cm, shorter than the right. In view of the considerable displacement of the original fracture and the marked shortening of the limb, lengthening of the fractured femur by overgrowth has taken place. (Pavlik, J. Bone & Joint Surg.)

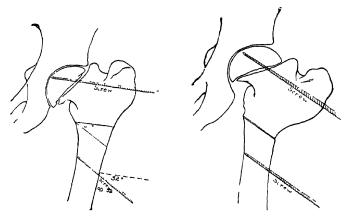


Fig 39—A, Left. The proximal screw should be inserted at a right angle to the femur, and the distal screw at an angle of 90 degrees, minus the angle around which the fracture line is to be rotated. B, After the osteotomy the 2 screws are parallel (Karfiol Surg, Gynec & Obst)

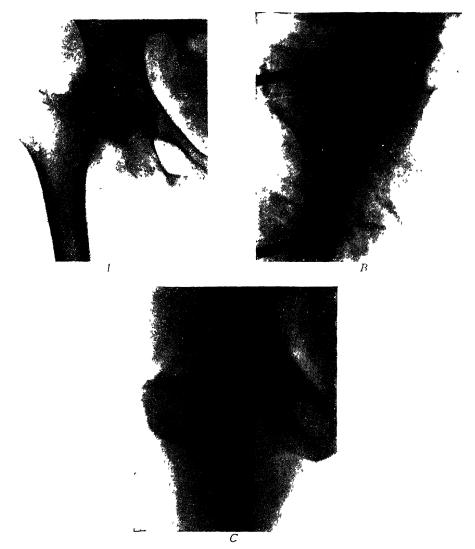


Fig 40—Case 2. A, Roentgenogram showing the patient's condition before operation, $2\frac{1}{2}$ years after injury B, Roentgenogram taken $5\frac{1}{2}$ weeks after operation C, Roentgenogram taken 15 months after operation. (Karfiol· Surg, Gynec & Obst.)

HERNIATED NUCLEUS PULPOSUS

Neurologic Aspects—The term herniated nucleus pulposus is used by R. Glen Spurling and F. Keith Bradford, 19 as it is believed that the disease of the

cleus pulposus were not unlikely to appear in neoplasm along the course of the sciatic nerve, rectal or pelvic disease and disease of the spine and innominate bone. On the bases of 85 cases of low intraspinal lesion, diagnosed and treated sur-

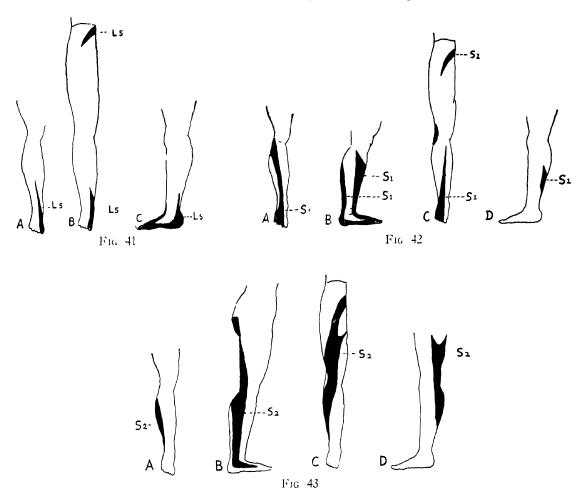


Fig. 41--Approximate derivations of the fifth lumbar root \mathcal{A} , Ventral view; \mathcal{B} , dorsal view, (, lateral view (Spurling and Bradford J. A. M. A.)

Fig. 42—Approximate dermatome of the first sacral root A, Ventral view, B, lateral view, C, dorsal view, D, mesial view (Spurling and Bradford J A M A)

Fig. 43—Approximate dermatome of the second sacial root. A, Ventral view, B, lateral view, C, dorsal view, D, mesial view. (Spurling and Bradford J A M A)

discs is rarely responsible for nerve root compression, except when the annulus fibrosus has ruptured and allowed the hermation of the nucleus to extrude through the defect.

Emphasis was placed on the fact that the history and neurological signs of nugically, the use of iodized oil in the spine was believed unnecessary as there was a characteristic clinical picture from a herniated nucleus pulposus at the fourth lumbar and lumbosacral discs.

Of special importance was the persistent sciatic pain exaggerated by cough-

ing, sneezing or straining Generally there was incapacitating low back pain preceding the onset of the sciatica by weeks, months or years. The onset of this back pain was usually associated with lifting or sudden torsion of the trunk in a bent forward position. This pain usually became more severe after several hours or days and was intensified by bending or lifting. Paresthesias were of more diagnostic value than the distribution of pain. Tingling, prickling, cold or numb sensations in the lateral aspect of the lower leg or foot were characteristic. Muscular weakness was not usually noticed as it was confused with the disability from pain, unless a palsy, such as foot drop, was present

A stiff lumbar spine was a prominent clinical finding. More important was the sciatic pain with the positive Lasègue sign, hypesthesia of the foot, lateral aspect of the leg and diminution or absence of the achillis reflex. Highly indicative of the lesion, but less frequently found, was the production of pain in the distribution of the sciatic nerve with pressure laterally on the spinous processes of the fourth and fifth lumbar vertebrae. A positive Naffziger sign (sustained pressure over both internal jugular vents) reproduced or accentuated the

sciatic pain in a fair percentage of the subjects with pain present on coughing or sneezing Occasionally weakness or paralysis of the peroneals, extensor hallucis, anterior tibial or extensor digitorum communis muscles was found. In some subjects fibrillation of the muscles of the leg was observed The sensory changes were the most important finding in establishing the diagnosis Testing with cotton wool or hot and cold test tubes revealed a definite area of hypesthesia more often than skin prick. Subjects with hermation of the nucleus pulposus at the fourth lumbar usually manifest hypesthesia of the anterolateral aspect of the leg with inclusion of the great toe Subjects with herniation at the lumbo-sacral manifest hypesthesia of the posterolateral aspect of the leg with inclusion of the lateral aspect of the foot This latter group generally showed loss of the achillis reflex. Sensory changes at times were found to extend to the posterior aspect of the thigh and the saddle region on 1 side

HIP

A New Method of Arthroplasty

Smith Petersen²⁰ describes a method of arthroplasty based on an entirely new



Fig 44—Preoperative roentgenogram of a case of bilateral ankylosis of the hip. Left, bony ankylosis, right, fibrous ankylosis. (Smith-Petersen: J. Bone & Joint Surg)

principle, in that of interposition of a mold by which nature can do its repair work. This mold is removed at a second operation thus leaving congruous joint surfaces which are capable of function

describes the vitallium mould which he employs at the present time. Numerous figures illustrate the various steps of the procedure including the preoperative x-rays showing the ankylosed hip, post-

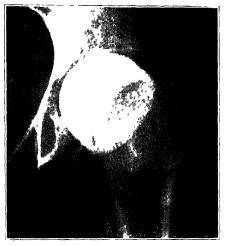


Fig. 45—Same case as shown in Fig. 44, 1 year after glass-mould arthroplasty of the left hip (Smith-Petersen $\ J$ Bone & Joint Surg)



Fig 46-Section from acetabulum (Smith-Petersen J Bone & Joint Surg)

because their covering approximates normal cartilage

The author describes his development of the mould, discusses the various materials used in this work and he finally operative x-rays showing the inserted mould covering the head and fitting into the newly constructed acetabulum, microscopic sections showing cartilage formation, *etc*.

This work promises to be one of the greatest contributions to arthroplasty. The author insists it is entirely too early to quote since the 29 cases on whom the vitallium mould has been used have all been operated on since June, 1938.

aged in which open operation is contraindicated. Twelve cases were reported in which extra large Smith-Petersen nails were inserted by x-ray guidance. Relief of pain was obtained in nearly all of the cases.

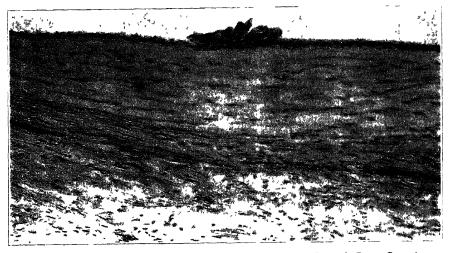


Fig 47—Section from capsule (Smith-Petersen. J Bone & Joint Surg)



Fig 48—Section from femoral head (Smith-Petersen J Bone & Joint Surg)

Fixation of Osteoarthritic Hips by Nailing

Bunns²¹ describes a simple procedure of fixation of osteoarthritic hips in the

HUMERUS

Supracondylar Fracture — Siris²² analyzed 330 cases of supracondylar fractures of the humerus treated on the

Surgical Service at the Bellevue Hospital over a period of 18 years, 292 of these cases were followed for study. Fortynine per cent occurred between the ages of 5 and 7 years. In 22 per cent there was no displacement of the fragments. In 74 per cent there was posterior displacement of the distal fragment. In 4 per cent there was anterior displacement of the distal fragment. There were no cases with a separation through the epiphyseal plate. In 6 per cent, however, the line of fracture extended into the epiphyseal cartilage.

The treatment was based on 4 objectives First, prevention of Volkmann's paralysis. Second, a satisfactory reduction. Third, the prevention of a varus or valgus deformity Fourth, the restoration of function. A general anesthesia was regarded important in order that the subjects be completely relaxed before manipulation was attempted. Local anesthesia was only warranted when general anesthesia was contraindicated. The fluoroscope was only used to check position following manipulation and not for visualization during the manipulation. Two cases had received x-ray burns from prolonged fluoroscopic reduction. In correcting the posterior displacement of the distal fragment it was essential that the lateral deformity be taken into account If there was any impaction in lateral displacement this was broken up by rocking the fragments. Gentle pressure between thumb and index finger on the condyle aligned the fragment on the long axis of the humerus The elbow was then hyperextended and downward pressure was exerted on the lower fragment as advocated by Lusk Then the elbow was flexed, after the method of Jones, and the forearm pronated, as emphasized by Boehler. After an x-ray check on position of fragments immobilization was accomplished by an anterior and

posterior moulded splint. A crescentic opening was always cut out at the distal end of the lower splint so that the radial pulse could be determined. Any failure of the patient actively to flex and extend the fingers was regarded as the first intimation of a neurovascular disturbance which might lead to a Volkmann's ischemic paralysis. Such a circulatory disturbance was not encountered in this series, except when reduction had not been obtained or maintained. were 8 cases in which suspension by means of a Thomas splint with skeletal traction was used to avert this complication. Caution against the prolonged use of suspension was necessary to prevent nonunion or excessive callous formation.

The splinted arm was suspended in a sling from the patient's neck. At the end of 2 weeks the splints were removed and the forearm was placed in a sling with the elbow at a right angle. Passive motion and physiotherapy were not used. Active motion by the patient through a limited range was considered the best way to restore function. Occupational therapy was recommended for this. The author expressed a preference for an adhesive dressing, over plaster splint, to hold the arm in flexion with the forearm pronated as this permitted a limited range of active motion during the early splinting period This dressing was not recommended for general use because of the particular care necessary in its application to avoid possible constriction

An open operation was done in but 1 case which was complicated by a loose articular fragment. The roentgenogram could not be relied on as an indicator for surgery, as the reparative powers of the child under proper supervision were to be considered. The trauma of surgery in children was always followed by an excessive amount of callus which resulted in impairment of function.

In the anterior displacement of the distal fragment there were no circulatory disturbances. Only one was compound. In 5 the forward displacement could not be reduced. The end results of the latter were comparable to those in which reduction was obtained. The author does not believe, however, that a principle of allowing the distal fragments to remain displaced has any foundation from this observation.

Cases which healed in a varus or valgus deformity or developed such a deformity as a result of damage to the epiphyseal plate were treated by cuneiform osteotomy some months or years after fracture. Myositis ossificans traumatica was not encountered in this group of cases which had no physiotherapy. The author stressed his view that massage and passive motion were attributable factors to this complication



Fig 49-Moderately advanced Kienbock's disease (Cave J. Bone and Joint Surg.)

In the compound fractures it was stressed that the most important first aid teaching was against any traction which might disturb the projecting fragments But I case was compound on the posterior surface of the elbow and this was due to avulsion of the skin In all a débridement of the wound was done Primary suture or Carrel-Dakin technic were used depending upon the extent, type, and duration of the wound The final results in the 12 cases of compound fractures were complete function in 10, fair in 1 and ankylosis of the elbow in 1.

KIENBOCK'S DISEASE OF THE LUNATE

Cave^{2,3} states that this disease occurs characteristically in young adult males who are engaged in laborious occupation. The onset is insidious and frequently no history of injury can be recalled by the subject. Pain is usually slow in onset with a definite increase resulting in moderate stiffness and thickening of the wrist joint. Symptoms are made worse by use and improved with rest and support. Sudden or forced motions bring on severe pain. The wrist appears swollen and thickened in the antero-

posterior diameter. This is most marked over the central portion of the dorsum of the wrist. There is acute local tenderness sharply localized in this area. Limitation of motion is present but varies in different individuals. Generally, dorsi flexion or palmer flexion and ulnar deviation are limited Shortening of the third metacarpal could at times be noted when the hand was clinched and tapping over the head of this bone produced pain in the region of the lunate. The diagnosis depends upon the x-rays It differs from tuberculosis in view of the fact that other carpal bones are not affected or changed in appearance

The treatment varied according to the length of time which symptoms had existed and the appearance by x-rays A support of plaster or leather wristlet was recommended in cases which showed no change by x-rays or who had symptoms for but a few weeks When the lunate was permanently deformed and appeared as an irregular sequestrum or had disintegrated, it was excised. Of the 5 cases reported, 4 cases were treated in this way. Two were back at their former occupation. Mouat, Wilkie and Harding previously reported excellent results in 6 of 7 cases subjected to surgical removal

LEG LENGTH

A Clinical Consideration of the Methods of Equalizing—Wilson and Thompson²⁴ have thoroughly reviewed the method employed in equalization of the length of the 2 lower extremities, Their conclusions are as follows.

- 1 Local stimulation of bone growth has not as yet been proved sufficiently successful to warrant clinical application
- 2 Lumbar sympathectomy when indicated for the correction of circulatory

disturbances in association with inequality of leg length, as frequently seen in poliomyelitis, may be expected to cause a favorable alteration of the diminished growth rate of the shorter extremity. Even when done before the age of 9 years, improvement cannot be assured, and the greatest gain that can be expected is approximately 1 inch.

- 3. Epiphyseal arrest in comparison with the other operative methods has the advantage of being a relatively minor surgical procedure Few, if any, complications need be anticipated. Careful calculation is necessary to determine the age at which the operation should be performed, and which epiphyses should be fused This depends upon the age of the patient when first seen, the amount of shortening and whether or not it is increasing. When a gross discrepancy of length is to be overcome, the operation must be performed early Complete fusion must be obtained in order to avoid any danger of later deformity due to asymmetric growth This method offers the simplest and safest means of equalizing leg length. Its only drawback is that its application is limited to the growing period
- 4 Leg lengthening is a formidable procedure and frequently attended by serious complications. Until these difficulties have been overcome, its use should be limited to patients who are too old for epiphyseal arrest and are unwilling or ill able to sacrifice height by undergoing shortening of the longer extremity. Previous infection of a bone of the shorter extremity is a definite contraindication. We also warn against undertaking this procedure in a severely paralyzed or atrophic extremity.
- 5 **Leg shortening**, like epiphyseal arrest, has the disadvantage that it must be undertaken on the longer and usually normal leg. It is a relatively simple and

safe procedure. Serious infection, nonunion, deformity and muscle weakness have not been reported. Although the operation has been performed almost exclusively upon the femur, it has also been undertaken successfully in the lower leg. The maximum correction so far reported is approximately 3 inches Leg shortening should be advised only when growth is well established. Many patients show an aversion to loss of stature, but the elimination of the raised shoe more than compensates for this Furthermore, it should be pointed out that a lowering of the center of gravity in a patient with a crippled lower extremity usually results in a gain of stability and an improvement of locomotion. Leg shortening, therefore, has the advantage over leg lengthening, in that it actually improves function

LOW BACK AND SCIATIC PAIN

Intraspinal Causes—Bradford and Spurling²⁵ report the results encountered in 60 consecutive laminectomies performed. Of the 3 pathologic conditions described the hermated nucleus pulposus is by far the most frequent, occurring in 35 of the group. Tumors of the cauda equina were encountered in 3 cases Hypertrophied ligamentum flavum was encountered in 13 cases, 9 of the group the operative findings were entirely normal. Lesions low in the spinal canal are the commonest single cause of recurrent or chronic low back and sciatic pain in that group of patients in whom any bony disease of the lower spine is demonstrated

LOWER JAW FRACTURES

Mandibular fractures occurred most frequently in jockeys, steel workers, sea-

men and stevedores. Robert P. Bay and Brice M. Dorsey²⁶ further observed that the common fracture sites were the junction of the body and ramus, the bicuspid region, the molar region and the symphysis. A condyloid process fracture usually accompanied a fracture of the mandible or the opposite side.

The diagnosis was made from history of traumatic injury, pain, swelling, improper occlusion of teeth, partial loss of function, abnormal mobility, crepitus and radiographic evidence

The treatment was reduction as soon as possible When teeth were present, a small loop of wire was passed through the space between the teeth so that one end was on the linguinal side of the first bicuspid and the other on the linguinal side of the second bicuspid. The loops were then firmly twisted together. The same procedure was carried out on the opposite side and also at corresponding sites on the maxilla. Pieces of wire were then drawn through the evelets so that the maxillary and mandibular teeth on each side were brought into occlusion, The maxilla thereby acted as a splint for the mandible. The wires have a tendency to stretch and must be tightened every few days

If upper and lower teeth were missing, a piece of dental impression compound was placed over the fracture site. The mouth was closed and the fragments manipulated into position. The compound thereby being moulded to hold the position. When upper teeth were missing, the teeth on the denture could be used for fixation of the lower jaw.

In edentulous mandibles, the fracture was repaired by open reduction. This could be done under local anesthesia. The oral cavity was cleansed. All remaining roots and salivary calculi were removed. The tooth in the fracture line was always removed. The fracture ends

were fixed by means of a wire suture passed through drill holes. Then the mucous membrane was closed with black silk. Osteomyelitis was rare but when it occurred, incision was best done extraorally. A liquid diet to give sufficient Calories must be planned for the patient.

NERVES

Delayed Paralysis From Single Muscular Contraction

Nielsen²⁷ called attention to paralysis developing a few days subsequent to a sudden muscular contraction. muscular contractures resulted from a fall, stumble, or sudden effort of the subject to catch himself in avoiding a fall The external peroneal was involved in the lower leg and the long thoracic nerve and the right dorsal scapular had been involved in the shoulder region. The physiology of this paralysis was described as that of a crushing of the nerve at the time of the sudden muscle contracture. Important points in diagnosis of such a condition were some sensory discomfort in the affected area at the time of injury with a recurrence of that discomfort some hours or days following, and the appearance of paralysis within a few months. The treatment consisted of physiologic rest by means of *splint* or brace and physio-therapeutic measures to prevent muscle atrophy until there was recovery of the nerve.

Horse Serum Neuritis

Bennett²⁸ states that horse serum neuritis, a severe sequel of serum sickness, develops at the height of the serum disease usually 1 week after the injection of serum. Any type of horse serum can produce it, but most cases follow tetanus antitoxin. The neuritic type of pain is

classic, and an early diagnosis of the complication can be made.

The etiology is unknown. Perineural edema giving compression neuritis seems the logical cause. In a large majority of cases a peculiar anatomic localization occurs, 5 to 6 per cent brachial plexus. About 115 cases have been reported in the world literature during the past 30 years.

Ideal treatment would be prophylaxis of serum sickness by substitutions of other serums for horse serum. Treatment is by *dehydration*, and *splint* in acute phase

Prognosis for recovery is usually good within 6 months. Twenty per cent of the cases were left with residual weakness and atrophy. Medicolegal responsibility in industrial or compensation cases must be recognized.

OSTEOMYELITIS

Acute Hematogenous Osteomyelitis of the Long Bones

Brown²⁹ reported 160 cases of acute osteomyelitis compiled from the records of 7 hospitals He classified his results according to toxicity of patient and time of operation A patient with a temperature over 102° F (39° C) was regarded as toxic Operation was classed as immediate when performed within the first 48 hours and delayed when performed after the second day. In the toxic group with immediate operation the mortality was 34 per cent, against 11 per cent when surgery was delayed. In the nontoxic cases there was no difference in the mortality rate whether the operation was immediate or delayed Operations done in the presence of blood stream infection resulted in a 51 per cent mortality (The editors believe that septicemia alone could account for the

CONTRASTING TABLE OF OSTEOMYELITIS IN CHILDREN AND ADULTS

	Children	Adults
Onset	Acute, fulminating	Gradual
Pain	Excruciating from the onset	Marked but not well localized, increasing in intensity
Temperature and white blood cell count	Very high	Usually moderately elevated
Preceding infection and trauma	Usually present	Usually absent
Roentgen findings	Early picture normal, after several weeks' extensive involvement, with sequestrums	Early picture normal, after several weeks' involvement relatively localized, without sequestrums
Method of extension	From metaphysis through haversian system, subperiosteal abscess	Not through haversian system, no subperiosteal abscess

high mortality) If a secondary blood stream infection developed following operation a 52 per cent mortality occurred. The autopsy in the toxic cases, in which death followed early operation, proved by the evidence of multiple abscesses that the surgical procedure on the local bone lesion was futile. It was tound that the incidences of secondary foci in bone were 34 per cent following early operation and 21 per cent following delayed. There were no sequestra formed in the presence of a pure streptococcic infection. There was no significant difference in the percentage of cases developing sequestra in regard to early or delayed operation. In comparing the use of the drill and the gauge, a higher mortality accompanied immediate drilling. This was believed due to the more toxic state of the subject when the drill was employed. There was no difference in the number of secondary foci whether drill, gauge, or incision and drainage was done

Acute Osteomyelitis of the Long Bones of Adults

Zadek³⁰ reported 9 cases of adults with a primary osteomyelitis in a long bone. The femur was most frequently

involved. The onset was insidious It was generally difficult to discern an etiological trauma or infection. Pain was the most constant symptom. The temperature elevation at the outset was often nil The leukocyte count was but slightly elevated Both temperature and leukocytes might later become elevated. The pathologic changes occurred mostly in the diaphysis and were medullary or perios-The involved portion contained granulation tissue and purulent exudate The extension of the abscess was through the medullary cavity and when in the metaphysis would invade the neighboring joint. Sequestra formation occurred in but 1 case

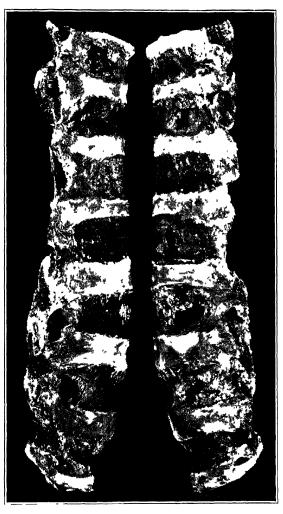
Treatment — This was surgical removal of a window of cortex 2.5×2 cm, as soon as the lesion was recognized. The aftercare was in accord with the Orr method (vaseline pack and closed plaster case).

Coccidioidal Osteomyelitis

McMaster and Gilfillan³¹ conducted a study of 24 cases of coccidioidal osteomyelitis. They found the condition was frequently misdiagnosed as either a pyogenic or tuberculous lesion. The disease was caused by a specific fungus, Cocci-

dioides immitis. The adult form of the organism was a sperule varying from 5 to 60 microns in diameter and was found in animal tissues. It released endospores when ruptured which were capable of forming into adult sperules. These, if

lesions were uncommon, it was not considered a portal of entry. A bite of an insect was a possible source of infection. There was no evidence of transmission from patient to patient. Thirteen of the subjects studied died. All had an asso-



log 50—(1088 specimen showing cavities of bone destruction, practically no collapse of the vertebral body and preservation of intervertebral cartilage. Large paravertebral abscesses were present. (McMaster and Gilfillan. J. A. M. A.)

grown in culture mediums, would develop into mycelia. The mycelia did not develop in animal tissue but could again form endospores. An epidemic region appeared to be the San Joaquin Valley in California. The organism gained entrance into the body through the respiratory tract or the skin. As gastrointestinal

ctated pulmonary focus. Ten of these cases had multiple osseus lesions. The 11 subjects who survived were studied from 2 months to 7 years after discharge from the hospital. Only 2 of them had minor lung infections. Five of this latter group had multiple bone or joint infections. There were but 4 patients under

20 years. Practically all bones of the body were found to be involved. The most commonly affected were tibia, vertebrae, sternum, tarsal bones, humerus, skull, fibula and radius. Four subjects had a primary localization in the synovial membranes of the joints but generally the joints were involved by direct extension.

area associated with marked swelling of superficial tissues. The early lesions were primarily destructive. There was no surrounding bone production or demonstrable periositis. In later lesions a fairly sharply outlined wall about a cyst cavity was found. In joints, the neighboring cartilage was destroyed and an ankylosis resulted (Fig. 53). Path-



Fig. 51—End result of coccidioidal infection showing bony fusion between with and sixth cervical vertebral bodies as well as laminas and spinous processes. This patient was treated only by immobilization. (McMaster and Gilfillan. J. A. M. A.)

Roentgenologically the lesions were found to occur in regions of cancellous bone. In long bones the lesions were apt to be in the metaphysis. The epiphyseal cartilage, when present, offered no obstacle to the progression of the disease. The cortical bone overlying a cancellous infection was destroyed by direct extension. Lesions of the sternum and scapulae showed a destructive

ologically there was little or no evidence of any production of tissue in the surrounding bone. The cortex was partly destroyed with an associated abscess of the soft tissue. The more chronic lesions appeared with an abscess cavity filled with soft or firm granulation tissue or spongy bone with interspaces containing grayish granulation tissue. In regions of liquified necrosis there was occasionally

palpable bony "sand." Infrequently, large sequestra were reported. The periosteum was thickened in the region of a cortical destruction. Infected joints showed a gray thickened synovia. The free fluid was serous or seropurulent. Articular cartilage revealed a marginal erosion by granulation tissue and segments of thunned articular cartilage could be found

mobilization of the local lesion, was indicated. Chronic infections in which bone abscesses were present were treated by surgical drainage, saucerization of the bone with the removal of the surrounding infection. The lesion was then handled like osteomyelitis, packing the bone cavity with petrolatum gauze and immobilizing the part in plaster



big 52-Appearance of typical coccidioidal infection of tibial tubercle. The lesion is essentially destructive. Note the periosteal reaction along the tibia. (McMaster and Gilfillan. J. A. M. A.)

separated from the underlying cortex by hyperemic granulation tissue.

Microscopic studies revealed the granulation tissue to be composed of round cells, polymorphonuclear leukocytes, histocytes, vascular spaces, Langhans giant cells and occasionally typical "tubercle formation" and the coccidendal sperules

Treatment — If there was an associated active pulmonary lesion, this received the primary attention. For the bone and joint lesions general supportive measures, as well as rest and imcast after the method of Orr. Joint lesions only healed with ankylosis; therefore, prolonged immobilization of the infected part until ankylosis was advisable. Amputation had been done in 3 cases with lesions of foot or ankle. No specific medication appeared successful A coccidioidal vaccine had been used without promise.

Hematogenous Pelvic Osteomyelitis

Management — Kulowski³² states that the local lesion was of a hemotoge-

nous origin, therefore, the systemic infection demanded the primary consideration. The uncertainty of the immediate conclusive diagnosis and the severity of the general infection which made the course of the disease unpredictable, precluded immediate surgical intervention. Para - osseous abscesses

inferior portion of its capsule into the iliopsoas or subiliacus space. Pus from the ischium filled the subgluteal space and occasionally the ischiorectal fossa. Less frequently burrowing along the ascending ramus of the ischium to the groin, scrotum or vulva. Suppuration in the pubis involved the space of Ret-



Fig. 53—Bony ankylosis of tibroastragalar joint following conservative treatment by immobilization in a plaster cast. (McMaster and Gilfillan. J. A. M. A.)

dominated the pathological picture. They masked the bony lesion and frequently spread out of fascial bounds by expansive dissection. Suppuration occurring from the posterior segment of the bony pelvis generally collected in the iliopsoas or subiliacus space. These emerged below the greater sacrosciatic notch or above the brim of the pelvis in the retroperitoneal tissues. Purulent exudate from the sacroiliac joint perforated the antero-

zius or Scarpa's triangle, and the adductor region. Pus from above the iliopectineal line formed a typical abscess in the internal iliac fossa.

In the second and third weeks an iliac lesion was distinguished in the x-rays as a pale moth-eaten island with marginal condensation. Sequestration was not as infrequent as would be indicated from previous reports. Ischial sequestra frequently were lying in a bed of infected

granulation tissue. Sequestra from the sacroiliac joint were generally situated anteriorly. There may be an associated loss of joint cartilage with obliteration of the joint and sclerosis of the opposing bone.

Extension by bony contiguity belongs to the later neglected stages This is

In a majority of cases the staphylococcus was recovered from the blood stream and the local lesion. The course of the infection was varied. An abortive type undoubtedly occurred in which there was no suppuration On the other hand, suppuration frequently occurred after the manifestations of the acute illness had



Fig. 54.—Gross specimen of amputated leg showing infection of synovial membrane of ankle with marginal destruction by exceedingful granulation tissue. (McMaster and Gilfillan: J. A. M. A.)

particularly true of the supracotyloid and infracotyloid juxtra-articular foer which extended into the acetabulum giving hip joint complications. Extension from the sacroiliac joint might lead to hemipelvic or lumbo-sacral involvement. At times a medial sacral invasion could determine a fatal outcome from meningeal involvement.

subsided Not infrequently it was found that sequestra were formed in the absence of any suppuration whatsoever, and again, during the acute course of the disease, suppuration and sequestration could occur.

Suppuration during the acute stage without any sequestration was a very frequent finding

Diagnosis in the acute stages was difficult because the initial lesion was subordinated by systemic reaction. Pain was frequently referable to visceral, retroperitoneal structures or hip joint. The profound toxemia, the absence of relief and the continued pain and positive blood culture were typical of the condition. The hip joint was generally maintained in a characteristic position.

confirmed by vaginal or rectal examination and focal aspiration, proved the diagnosis.

General infection was treated until definite suppuration had occurred. Iliopsoas and subiliacus abscesses were drained by an incision along the anterior superior border of the ilium. The subgluteal abscesses were drained lateral to the subgluteal space. Sacroiliac abscess

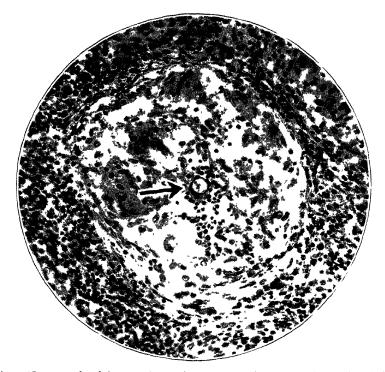


Fig. 55—Coccidioidal spore (arrow) present in the center of a "tubercle" (McMaster and Gilfillan J A M A)

for the lesions which were juxta-articular. Where there was focus in the ilium, the thigh was held in flexion and abduction. With a lesion in the sacrollac region the thigh was maintained in flexion. With an ischial focus the thigh was held in external rotation and abduction. With a pubic lesion the thigh was held in flexion, adduction and internal rotation. The eccentric limitations of hip joint motion and negative aspiration of the joint generally indicated an acute osteomyelitis of the pelvis. Infiltration, fluctuation and circumscribed tenderness.

generally was reached through the sacrosciatic notch or Petit's triangle. In the late stages for radical operative work required in removal of sequestra, more extensive meisions were used. For lesions of the ilium a Smith-Petersen incision reflecting the external soft tissue flap down to the margin of the acetabulum was used. For lesions of the sacroiliac joint the exposure was the same used in a Smith-Petersen fusion of the sacroiliac, resecting the block of ilium overlying the joint. For lesions of the ischium a posterior incision was used

through the gluteal fold retracting the gluteus maximus muscle upwards and laterally.

Hypovitaminosis and Osteomyelitis

This association was pointed out by Wachsmuth and Heinrich.³³ They described the experiments of Takahashi which demonstrated the resistance toward bacterial infection was reduced when there was a deficiency of vitamins A, B and C. In C avitaminosis, metastasis in the long bones was especially apt to occur. Intravenous administration of staphylococcic suspensions resulted in 100 per cent metastases in the bone marlow in the avitaminotic animals as compared with 444 per cent in the controls. The lack of vitamin C especially caused a locus minoris resistentiae at the end of long bones, which site was particularly subject to infection. A clinical case of streptococcic osteomyelitis following scarlet fever in a male 24 years of age was reported Four months after the acute illness the subject was found by roentgenograms to have sequestra in both radu and tibiae There were no clinical signs other than slight swelling at the sites. The sequestra were removed and hemolytic streptococci were cultured Noteworthy was the symmetrical involvement following a starvation diet or hypovitaminosis for 5 weeks

PATHOLOGICAL FRACTURES

Management—Investigation of pathological fractures by Bick³⁴ was based on a study of 85 fractures in 59 cases and additional specific case reports of fractures occurring in lesions not represented in the series

Fragilitas Ossium — The fractures healed rapidly with exuberant callus after simple immobilization or traction. The

fracture site, however, remained weak as was the prefractured bone.

In 12 subjects with metastatic carcinoma none showed any deposition of callus or other evidence of union. In other reports, however, the fractures have healed. The treatment consisted of simple immobilization in plaster or traction, depending upon type and location of fracture Radiotherapy applied locally has relieved pain in most cases

In 7 cases of bone cyst, 3 were allowed to heal spontaneously. In 1 the cyst failed to fill in and remained 1½ years unchanged after the fracture. In the cases in which curettage and bone chips were used, healing and regeneration within the cyst followed rapidly

In giant cell tumors, curettage and filling of the defect with bone chips, followed by plaster immobilization, was the most certain method of treatment.

In rickets, immobilization and intensive doses of vitamin D invariably let to early firm union. Without anti-rachitic treatment, the healing was retarded and the callus was "relatively soft."

In Gaucher's disease the fractures of the long bones treated by immobilization united after a prolonged period One case of delayed union resulted after 14 months and surgical intervention was resorted to

In the *spinal fractures*, *immobilization* by a brace resulted in healing with a deformity.

In Paget's disease all fractures healed well following simple immobilization or traction.

In chondroma it had previously been reported that no fractures healed until the tumor was excised. All cases healed rapidly with regeneration of the lesion following curettage and insertion of bone chips.

In localized osteitis fibrosa cystica regeneration proceeded much more rapidly

when curettage and insertion of bone chips was done

In osteogenic sarcoma 2 of the 3 patients showed evidence of healing before death. It was felt advisable to use plaster immobilization and radiation to palliate pain. The latter, however, does not contribute to the healing.

In the *neuropathies*, such as paralysis agitans, tabes, syringomyelia, etc., healing took place in normal time following *immobilization*. It was thought advisable, however, that a prolonged period of protection be observed against refracture.

In osteomyelitis, it was stated that the fractures would heal with simple immobilization when the osteomyelitis was in the regressive or healing stage. When the infection was actively progressive, it would destroy the newly formed bone more rapidly than callus could be deposited. Fracture was regarded as an inexcusable complication which occurred most frequently following extensive saucerization which weakened the structure of the bone.

In endothelial myeloma, hypernephroma and multiple myeloma union was rare Radiation was used as a palliative measure, in addition to simple immobilization

In syphilis, immobilization or traction, supplemented by antiluetic measures, resulted in complete restitution of the bone structure in normal time

In fibrosarcoma a case was cited which involved the upper end of the femur. This was excised and bone chips were inserted. Nine months later the fracture was united. Generally, however, the treatment would be the same as that for osteogenic sarcoma

In *osteopetrosis* union occurred following conservative care but recurrences were frequent

In multiple spontaneous idiopathic symmetrical fractures, osteoporosis my-

elolytica, no clinical union occurred and a slow dissolution of the fracture ends proceeded.

In osteomalacia union was reported as occurring as rapidly as in fractures of normal bone.

In *senile atrophy* the union was the same as that in normal bone.

PELVIS

Dislocation and Fracture Dislocation Treatment of Fractures

R. Watson Jones³⁵ divided pelvic injuries into 3 groups: (1) Isolated injuries of the pelvic ring (Fig. 556, p. 773), (2) combined injuries of pubic segment of the pelvic ring, (3) combined injuries of the iliac and pubic segments of the pelvic ring. The mechanics of displacement in pelvic fractures was likened to "an oyster on end"

The treatment of a complete dislocation of the symphysis and the sacroiliac joint without visceral complications was a reduction under general anesthesia. The subject was placed on the uninjured side with the trochanter lying on the pelvic rest of the fracture table. The 2 lower limbs were held by an assistant one abducted above the other. The reduction frequently occurred spontaneously At other times pressure over the iliac crest of the dislocated illum to push and rotate it downward and forward into line with the normal half of the pelvis was necessary. The double leg spica was left on for 3 months

Those fractures complicated by bladder and urethral injuries were nursed on their side if conditions did not permit reduction. It was noteworthy that considerable displacement of the pubic could exist without symptoms, but the same was not true with sacroilacs.



Fig 56—Isolated injuries of the pelvic ring. There is no displacement, no special treatment is necessary (Watson-Jones Brit J Surg)

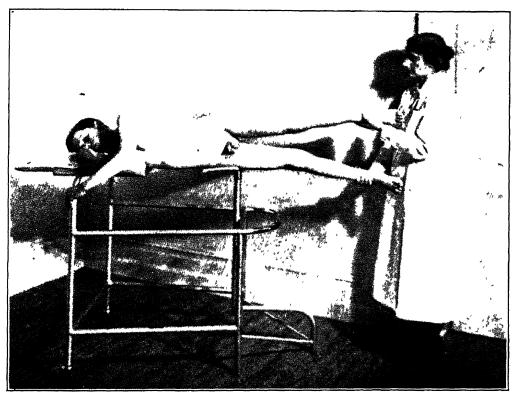


Fig 57—Reduction of dislocations and fracture-dislocations of the pelvis by lateral recumbency. (Watson-Jones Brit. J Surg)

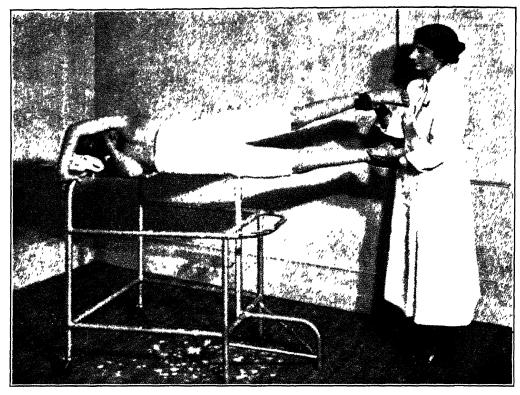


Fig 58—A double plaster spica is applied (Watson-Jones Brit J Surg)

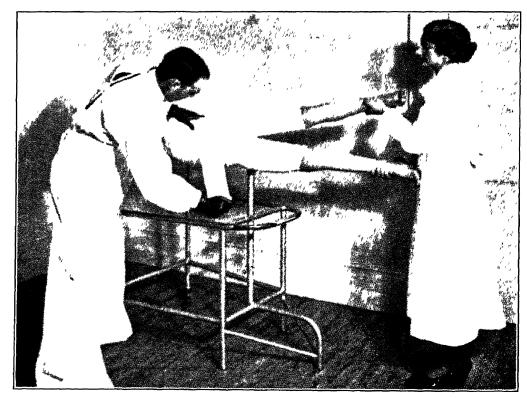


Fig 59—The dislocated ilium is rotated forwards and downwards towards the uninjured side (Watson-Jones Brit J Surg)

Treatment of Fractures

An analysis was made of 148 cases of fractured pelves by S. M. Leydig and J. Albert Key.³⁶ Seventy-eight per cent of these were injured in automobile accidents, 70 per cent were multiple fractures and 75 per cent were fractures without displacement of fragments.

The treatment of fractures of the pelvis was divided into 2 considerations. First, the care of the complication. Sec-

veins and injuries of sciatic nerve. There were no instances of damage to the great vessels. In the majority of cases in which there was no displacement of fragments, the patients were kept in bed with no specific treatment.

During the first week, the pelvis was very sore and movements were painful. A fracture bed was used with cross straps over the mattress so that the lifting of the patient on the bedpan was not

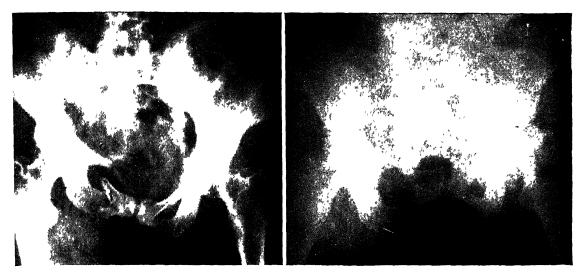


Fig. 60—Lett, Malgaigne type of fracture showing hemisubluxation of the pelvis. Right, Roentgenogram of same patient taken after reduction of the fracture by means of traction in a Hodgen splint. (Leydig and Key. Surg., Gynec & Obst.)

ond, the treatment of the fracture itself Shock was the most frequent complication in fractures of the pelvis due to violence which involved the production of such a fracture. This was responsible for a mortality of 7.8 per cent. Visceral lesions were next in frequency These were largely confined to the genitourinary tract. Next in frequency were the complications of fractures of other bones. These were treated as soon as the patient's general condition permitted it, but carried out with regard of the fact that the patient must be kept recumbent during the care of the pelvic fracture More rarely there were injuries of the rectum, thrombosis of the large necessary Pillows were placed under the knees to keep the thighs in slight flexion and a horizontal bar was extended from the frame above so that the patient was able to shift his position by lifting with his hands. Some cases were more comfortable with Buck's extension applied to the legs with some 5 to 10 pounds weight. The patient was moved to an ordinary bed in approximately 2 weeks' time but fracture boards were used beneath the mattress. The bedpan was permitted. Four to 8 weeks' bed rest was generally necessary.

Types of fractures which would require special attention were separations of the symphysis pubis, double fractures

of the ramii with displacement of the middle fragment and double vertical fractures of Malgaigne (through ramus of pubis and ischium with medial discanvas sling or hammock passed beneath the pelvis, the ends of which were close to the midline of the body in order to exert enough lateral pressure. There

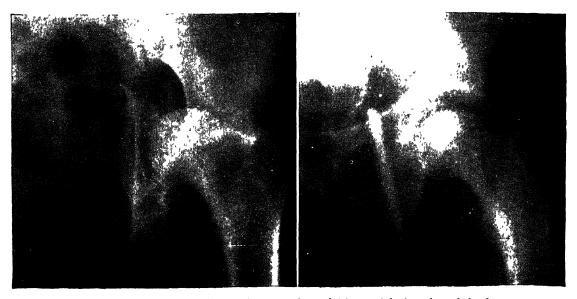


Fig 61—Left, Fracture of the acetabulum with partial intrapelvic luxation of the fragments. Right, Same after reduction by traction in a Hodgen splint and manipulation without anesthesia (Leydig and Key Surg, Gynec & Obst)



Fig 62—Central fracture of acetabulum with intrapelvic luxation of the head of the femur (Leydig and Key Suig, Gynec & Obst)

placement of the lateral fragment) and fractures of the acetabulum or central dislocations of the hip

In separation of the symphysis, lateral pressure was maintained by means of a

was rotation of the symphysis upward on 1 side and more traction was placed on that extremity In double fractures of the ramii, the patient was placed in the sling and traction applied to both

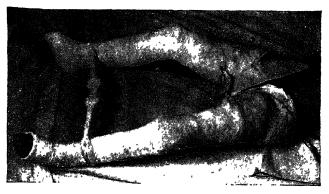


Fig 63—Illustration of cast with turnbuckle, applied to patient with fracture as shown in Fig 62. The dotted lines show the approximate position of the Steinman pins. (Leydig and Key Surg., Gynec & Obst.)



Fig 64—Final result after treatment in case (Same case as in Fig 63) (Leydig and Key Surg, Gynec & Obst)

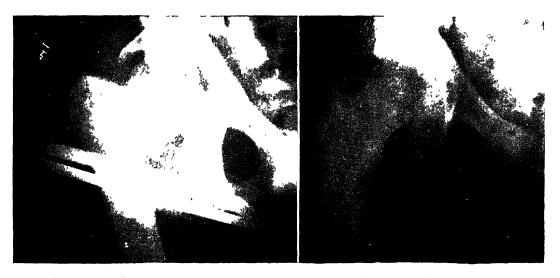


Fig 65—Left, Fracture of the anterior rim of the acetabulum Right, Result after open reduction (Leydig and Key Surg, Gynec & Obst)

lower extremities with them in a position of moderate abduction. In the double vertical fracture of Malgaigne a pull was exerted on the affected side in order to re-establish the leg length, hence the reduction of the fracture was accomplished either by well-leg traction splint or by use of a Hodgen's splint. The method of Watson Jones had not been used. In fractures of the rim of the acetabulum, it was found necessary to do an open reduction and suture the fragment in place, followed by immobilization in plaster-of-Paris spica for 6 weeks

There were 3 groups of acetabular fractures, those without displacement which were treated with traction of 10 pounds for 8 weeks. In the central dislocations of the hip it was not recommended that a finger be placed in the rectum in order to re-establish the position of the fragments. It was found much more advisable to apply traction and wait a few days to see if the dislo-

cation would reduce. Occasionally it was necessary to give the patient a general anesthesia and manipulate the hip with traction in line with the shaft of the femur and lateral traction on the upper portion of the thigh In 1 resistant case a turnbuckle was used between the upper ends of 2 leg casts which were stationary at the bottom. The effect of the turnbuckle was to spread the trochanters Note: In the editors' further apart opinion central dislocations of the hip are better handled with well-leg traction and transfixing the 2 trochanters with Steinman pins incorporated in the plaster on the well side, and the cast cut out on the involved side so that a stirrup can be applied to the Steinman pin to obtain lateral traction.

PES PLANUS

Operative Treatment—Young³⁷ described an ingenious procedure for opera-





Fig 66—A, Skeleton of the right foot from the superior aspect, showing position of drill hole and slot in the navicular bone B, Plantar view illustrating drill hole and slot from this aspect Attention is called to the shaded area which indicates the groove on the inferior surfaces of the navicular and first cuneiform bones (Young Surg, Gynec & Obst.)

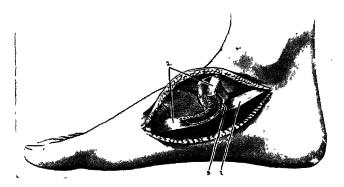


Fig 67—The tendon of the tibialis anterior muscle is looped through a drill hole in the navicular bone 1, Tendon of tibialis posterior, 2, tendon of tibialis anterior, 3, slot from drill hole to posterior part of medial aspect of navicular bone (Young Surg., Gynec & Obst)

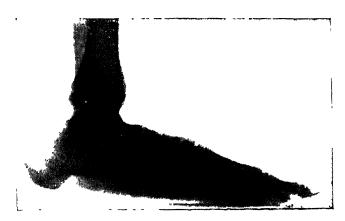


Fig 68—Case 3 Preoperative roentgenogram of right foot (Young Surg, Gynec & Obst)

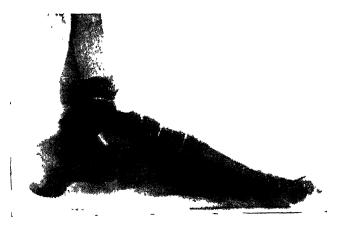


Fig 69—Case 3 Seven months after operation (Young Surg., Gynec & Obst)

tive correction of pes planus in cases not responding to conservative treatment. The procedure was used in 6 adolescent cases and 1 adult with symptomatic relief in all cases. The principle of the procedure is to change the pull of the tibialis anticus tendon directly to the tubercle of the scaphoid. A lengthening of the heel cord was first done. Then

hook the anterior tibial tendon was retracted posteriorly and introduced into the slot to assume a position in the drill hole.

RADIAL HEAD AND NECK

Resection—A follow-up study of 13 cases of resection of the radial head and



Fig 70—Case 5 Preoperative lateral view of right foot (Young Surg., Gynec & Obst.)

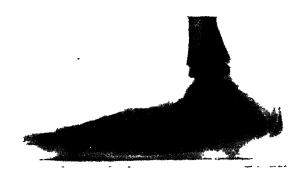


Fig. 71—Case 5 Four months after operation (Young Surg , Gynec & Obst.)

through an meision which ran from the base of the first metatarsal to beneath the internal malleolus, the scapho-cuneiform bones were exposed with the attachments of the tibialis posticus to the tuberosity of the scaphoid and the attachments of the tibialis anticus to the metatarsal cuneiform joints. A drill hole was then made anteroposteriorly through the scaphoid just lateral to the tuberosity. A slot was cut in the posterior portion of the scaphoid to join with the drill hole. Then by means of a button-

neck was made ³⁸ The average postoperative care for the group was 4 years
Nine patients were still in their growth
period when operated. Four were over
18 years. Pain, weakness or tenderness
at the elbow persisted in but 3 subjects.
Limitation of elbow motion was present
in 6. Two of these exhibited a complete
loss of pronation and supination due to
radial, ulnar ankylosis. Mobility at the
elbow was good in all cases. Increase in
normal carrying angle at the elbow appeared in 4 subjects. Formation of bone

at the operative site occurred in 4 cases which necessitated a second resection. Anterior luxation of the radial stump did not occur Pain, weakness or tenderness at the wrist was complained of in 5 subjects. Radial deviation of the hand occurred in 1 case. There was prominence of the ulna at dorsum of the wrist in 2 subjects. Three cases had limitation of motion of wrist. Proximal displacement of the radial shaft occurred in all cases, except those which had a synostosis Widening of the distal radioulnar joint occurred in all cases with a few exceptions mentioned above.

Resection of the radial head, therefore, was avoided in the growing child or adolescent. When removal was necessary all attached bone fragments and periosteal shreds were débrided. The use of a free graft of fascia lata approximated with pursestring sutures over the end of the stump was recommended to form a limiting membrane to prevent a synostosis. To avoid proximal displacement of the radial shaft and disability of the wrist joint, it was suggested that the annular ligament be repaired and the wrist immobilized in maximum ulnar deviation by means of a plaster cast from the base of the fingers to the elbow which would allow free pronation and supmation of the arm. This was to be followed by daily active and passive ulnar deviation stretching exercises.

SEMILUNAR BONE OF THE WRIST

Operation for Dislocation—If closed manipulation cannot be accomplished in dislocations of the semilunar bone of the wrist, Mahorner and Meade³⁹ use the anterior approach in open reduction, a curved elevator being inserted under the os magnum with pressure applied on the

lunate with flexion of the wrist. Five cases were reported with perfect results in 4 of them and 1 case of 18 months' duration had a poor result and removal of the semilunar bone was necessary.

SHOULDER JOINT

Pathology and Treatment of Recurrent Dislocations—Blankhart states that recurrent dislocation has nothing to do with traumatic dislocation. It is produced differently. The ordinary dislocation is caused by a fall on the abducted arm. In extreme abduction, the neck of the humerus impacts against the acromium process and then by leverage the head is forced through the lowest and weakest part of the capsule between the subscapularis and triceps.

The dislocation which afterwards becomes recurrent is caused, not by a fall on the abducted arm, but by a fall either directly on the back of the shoulder or on the elbow which is directed backwards and slightly, if at all, outwards. The humeral head is forced directly forward and shears off the fibrous or fibrocartilaginous glenoid ligament from its attachment to bone The detachment occurs over particularly the whole of the anterior half of the glenoid margin The reason why the dislocation recurs after the reduction is that, whereas a rent in the fibrous capsule heals readily and soundly, there is no tendency whatever for the detached glenoid labum to reattach itself to bone

The author has exposed this typical lesion at operation in 27 consecutive cases. It is a constant, straightforward, uncomplicated, anatomical condition. Briefly the operation is performed in the following manner: Anterior approach; coracoid process divided and reflexed down with 3 muscles, subscapularis sec-

tioned, bone of anterior glenoid denuded, and capsule attached.

All 27 cases have recovered full joint movement and in no case has there been any recurrence.

SPINAL CORD

Injury During Reduction of Fractures of the Vertebrae — Rogers³⁹ states that of 70 patients with fractures and dislocations of the thoracic and lumbar vertebral bodies treated by Rogers in the past 9 years, only 2 showed fracture dislocations and 2 showed crush fractures involving the posterior wall of the centrum with backward displacement of the bone fragments. In none of these 4 cases was there any evidence of injury to the cord or pressure on the nerve roots immediately after the injury In 3 cases paralysis developed as a result of treatment; in 2 cases of fracture dislocation during reduction and in 1 case of vertebral fracture 2 years after injury. In none of the other 66 cases, in which the usual wedge compression was present, was there the slightest evidence of pressure on the spinal cord or the nerve roots incident to treatment The author groups all fractures of the vertebral bodies, therefore, into 2 groups, the "safe" group, in which the fracture does not involve the posterior wall of the centrum (this represents 90 per cent) and the "dangerous" group, in which the fractures and dislocations involve the posterior wall of the centrum. It is essential, therefore, that the alignment of the articular processes be determined accurately before reduction is attempted. If there is lateral disalignment, the reduction should be open and flexion should be employed to disengage the locked processes Extension of the spine in such a case may injure the cord or

the nerve roots. Traction alone will not free the locked articular processes.

SYNOVITIS

Chronic Synovitis of Knee Joint

Treatment by Synovectomy-Inge reviewed 86 cases with chronic synovitis of the knee joint treated by synovectomy.42 Nine of these cases were the site of specific lesions in the synovial membrane Six were tuberculous synovitis in which a synovectomy had been performed because of a mistaken diagnosis In all 6 cases a rapid recurrence of the disease occurred which required an operative fusion of the knee subsequently The other 3 specific lesions were hemangioma of the synovial membrane, echinococcic disease and osteitis of the tibia Of the remaining 67 cases of chronic nonspecific arthritis of the knee, 19 had bilateral synovectomies. The cause of these lesions were rheumatoid arthritis, osteoarthritis and chronic proliferative synovitis (9 traumatic and 6 osteochondromatosis) In a follow-up period of 51/2 years' average, a satisfactory or improved result based on relief from pain and improvement in function was observed in 74 per cent. The best results were obtained with osteoarthritic joints with secondary synovial hypertrophy and effusion. Of these, 90 per cent obtained improvement. In rheumatoid arthritis symptomatic relief was obtained in only half the cases. In cases of chronic proliferative synovitis, due to trauma or osteochondromatosis, the improvement was the same as in the osteoarthritic group.

Villous Synovitis of the Knees Due to Improper Weight Distribution

Attention was called by W. H. Irish and J. P. Stump⁴⁸ to the fact that pro-

nation of the feet caused pain of the internal lateral ligament of the knee The internal lateral ligament of the knee was directly adherent to the capsule of the joint and any strain, therefore, placed upon it would result in reaction of the synovial tissue In subjects with weak and distorted feet, the weight-bearing line was thrown from the center and abnormal stress on the joint capsule and lateral supports caused the irritation of the synovial membrane which set up inflammatory process resulting in hypertrophy with proliferation of the villous formation. Characteristic of this disturbance were pain, disability and thickening of the knee with insufficient bone changes by x-rays to account for the symptoms. Symptoms generally progressed over a period of months. The pain was generally localized in front of the lateral ligaments or in the popliteal space. This was increased on walking or standing and particularly in descending the stairs. After rest the knees were stiff and the first motions caused increase in pain. The subcutaneous tissues were usually thickened and the knees appeared large and misshapened. There generally was no demonstrable fluid in the adult. Lateral instability was not pronounced, crepitation was the most general finding All subjects showed a moderate or severe deviation of the weight-bearing line from their pronated feet. The diagnosis generally could be confirmed by taping the feet in inversion with adhesive tape. A marked relief of symptoms followed in 2 or 3 days. It was believed that this was the type of knee which progressed to osteoarthritis

The treatment of the condition consisted in correcting the pronation of the feet with adequate shoeing with proper supports. Reduction of weight was most beneficial in the obese subject Deep heat and massage of the mus-

cles were necessary in the adult with joint changes. This was followed by exercises to develop the quadriceps.

THUMB, INTRINSIC MUSCLES

Royle⁴⁴ describes an operation to restore the opposing function of the thumb when there is paralysis of the intrinsic thenar muscles. The flexor sublimis muscle to the ring finger is used. This muscle is divided just beyond its bifurcation at the base of the finger, drawn back and out at the wrist and then passed up the sheath of the long flexor of the thumb and attached, 1 branch to the short flexor muscle and the other to the opponens pollicis Reduction is simple since attempting to flex the ring finger draws the thumb into opposition.

(Editorial Note—This operation seems simpler in technic than the other methods of tendon transplantation, most of which must utilize a tendinous pulley to secure pull in the correct direction)

TIBIA

Pseudofracture

Pseudofracture of the tibia is a clinical entity involving the upper third of the tibial shaft in children between the ages of 4 and 16.45 At 1 stage of the disease, the roentgenographic appearance may simulate a fracture, but acute trauma, nevertheless, is not an etiological factor

The exact nature of the disease is not known. There is a possibility that it may be due to a chronic infectious process. The pathological reports on 2 of the cases in which biopsies were done suggested this, as did the slight fever and leukocytosis present in 3 of the cases. Ollonqvist, in Finland, has reported a series of cases which simulate this condi-

tion. His cases, however, occurred in young army recruits, and in each case the lesion was in the middle third of the tibia instead of in the upper third. March foot is another condition that gives a similar roentgenographic appearance except for the location. The etiology of this latter condition, as well as that of the disease described by Ollonqvist, remains unknown Other authors have commented on what were probably lesions akin to pseudofracture. Several German writers speak of an "Umbauzone" and note its occurrence in other bones besides the tibia Reischauer calls them "wear-and-tear" fractures, due to active use of the limb, particularly in soldiers. We hope that study of the circulation in growing children may give some clue, as the roentgenograms suggest that the pseudofracture line may be influenced by the course of a nutrient arterv.

TUBERCULOSIS

Tuberculosis of Knee

McKeever⁴⁶ advocated surgical treatment in tuberculosis of the knee Initial surgical procedure consisted of the removal of synovial membrane, articular cartilage and the ends of the tibia and femur, care being taken to avoid the epiphyseal line. The tuberculous foci encountered were thoroughly curetted even when they crossed the epiphyseal line The study consisted of 47 patients. Fifty-five per cent presented clinical manifestations before the fourth year of life Forty-five per cent before reaching the tenth year. An average of 3 years conservative care per patient was tried and did not result in ankylosis of 1 knee joint There were 2 mortalities during conservative care, 1 after 2 years developed pulmonary tuberculosis, the other

after 1 year from tuberculous meningitis. One case came to amputation 3 years after illness. Sinuses developed spontaneously in 5 cases. Lumbar sympathectomy was employed twice. these subjects the clinical signs of activity increased rapidly. Resection "economical" was employed in 39 patients. 13 were between 6 and 8 years. The oldest in tenth year and the youngest 17 months The latter failed but was finally arthrodesed by a second operation in the tenth year. There were 2 mortalities as a result of the operation. One from a pulmonary embolus and the second an extensive cellulitis

Thirty-four patients could be followed from $1\frac{1}{2}$ to 13 years, 42 per cent of these were over 14 years of age Thirtythree had solid clinical and x-ray bone union. One, although quiescent, had pseudarthrosis. Fusion was successfully accomplished after 1 operation in 27 cases. Two operations were required in 3, 3 operations in 2, and 4 in 1. In the latter, the first attempt was made at 5 vears Two cases were operated on at the time the knee presented draining sinuses of long duration. In each case fusion resulted from the first operation The average shortening of 32 cases was 4.4 cm. The most shortening, that in a 16-year-old boy, who had been subjected to operation 9 years previously, amounted to 5 inches. The amount of shortening appeared to be in definite relationship to the amount of destruction of the epiphysis. In 1 case there was actual lengthening of 25 cm. A flexion deformity of the knee of less than 25° apparently was not disadvantageous. The greatest deformity was 60° corrected by osteotomy. The operation having been done at 9, correction at 12 The flexion deformity which resulted seemed to progress rapidly during the first 2 years following resection in spite of immobilization

Genu valgum deformity resulted in 6 cases. Five developed a varus deviation. Internal torsion of the tibia on the femur was present in 4 cases. Genu recurvatum occurred in 3. Twenty-cases required no corrective osteotomy.

Insulin in the Treatment of Bone and Joint Tuberculosis

Nichols and Compere⁴⁷ state that 15 cases of bone and joint tuberculosis. given from 2 to 5 units of insulin 20 minutes before each meal, showed an average improvement in their weight All the patients showed greater interest in their food. It was concluded that insulin could be used for patients with bone and joint tuberculosis who had poor appetites and who under the best environmental conditions did not gain weight.

XANTHOMATOUS TUMORS OF JOINTS

De Santo and Wilson⁴⁸ present a most complete review on this subject, listing the analytical study of 190 cases. The conclusions are as follows

- 1 Xanthomata of the synovial membrane of the joints are probably commoner than has been hitherto supposed, as is exemplified by this group of 9 cases over a brief period of time.
- 2 The preoperative diagnosis of joint xanthoma seems never to have been made. Obscure intermittent swelling of the knee jointassociated with pain and free fluid, occasional locking, and a movable tumor, usually medial to the patella-will frequently be found to be caused by xanthoma.
- 3 Aspiration of the joint with the recovery of dark or sanguineous fluid points to the presence of tumor. The demonstration of a large amount of cholesterol in the fluid is probably pathognomonic of xanthoma
- 4 Xanthomata originate in chronic hemorrhagic villous arthritis
- 5 The stroma cell is related to the reticuloendothelial system It is derived from the surface synovial membrane mesothelium, which

has reticulo-endothelial properties, and gives rise to: (a) The foam cell; (b) the giant cell, and (c) the pigmented cells found in xanthomatous tumors.

- 6. Joint xanthomata are related to some fundamental disturbance of lipoid metabolism. The blood cholesterol is frequently elevated.
- 7. Cholesterol formation probably takes place locally as a result of interstitial hemorrhage and is decomposition product of hemoglobin. Its failure to be formed universally when interstitial hemorrhage occurs is partially explained by the systemic disturbance of lipoid metabolism which usually exists.
- 8. Joint xanthomata can be cured by radical excision. In the case of solitary tumors, local excision is sufficient, but, in the case of multiple or diffuse xanthomata, a subtotal or total synovectomy is usually necessary
- 9. No instance of a benign giant-cell xanthoma undergoing malignant transformation was found.

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RADIOLOGY

By Robert Shoemaker, 3rd, M.D.

VISUALIZATION OF THE CHAMBERS OF THE HEART, THE PULMONARY CIRCULA-TION AND THE GREAT BLOOD VESSELS IN MAN

This was accomplished by G. P. Robb and I Steinberg¹ by developing a technic which would permit injection of a radiopaque substance rapidly enough to make the blood stream opaque. The radiopaque substance for this purpose must be (1) Freely miscible with the blood, (2) pharmacologically mert, (3) nonirritating to the vascular system, (4) nontoxic in the doses used, and (5) rapidly mactivated or eliminated by the body Diodrast, injected at a rate not exceeding 1 ounce (30 cc) per second has satisfied these criteria

Roentgenograms are made at the time the system to be studied is opacified The interval between injection and taking the films is judged beforehand by measuring the "arm to lung" and "arm to carotid sinus" circulation time to the right and left heart The technical factors for the films differs from the conventional only in the use of overpenetration An increase of 8 to 12 kv above the usual kilovoltage is usually sufficient With 1 injection and 2 roentgenograms provided by the ordinary cassette shifter for stereoscopy, it is possible to visualize the right side of the heart and the pulmonary arterial tree practically every time. The left cardiac chambers and the thoracic aorta are also visualized in about three-quarters of the cases

The dosage varies roughly with the body weight and the region to be visualized. In the average person, $1\frac{1}{6}$ ounces (35 cc) of the 70 per cent solution of diodrast is sufficient for opacification of the left heart and thoracic aorta; % to 1 ounce (25 to 30 cc) suffices for visualization of the pulmonary blood vessels. The duration of injection is 2 seconds or less.

Roentgenoscopic examination of the chest usually precedes visualization of the heart and aorta in order to record the optimal position of the thorax for the

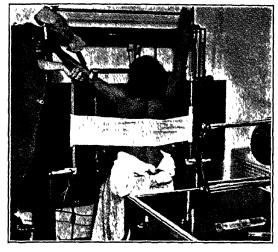


Fig 1—Posteroanterior position Note elevation of arms Injector protected by lead apron stands at side of casette shifter (Robb and Steinberg Am J Roentgenol)

right and left anterior oblique views. To test the correctness of the position and the roentgenographic technic, a control roentgenogram is made and developed at once

Next a modified 12-gauge Lindermann transfusion needle connected to a 2-way Luer-Lok stopcock having an inside diameter of 0.083 inches is inserted into an arm vein and the patient placed in position. A 50 cc syringe containing the proper amount of diodrast is connected and approximately $\frac{2}{3}$ ounce (20 cc.) of blood is drawn into the syringe slowly, to prevent diffusion. Being lighter, the blood rises to the top and with the arm raised to an angle of 45 degrees above the horizontal, it forms a column above the diodrast.

The patient is now ready for the injection. At the direction, "breathe out," he

exhales forcibly until stopped by the command, "breathe in." At this moment the stopwatch is started by the technician and the injection is begun. The contents of the syringe are injected in 2 seconds or less. The inspiratory position is held until the opaque material has arrived in the pulmonary arterial tree and the roentgenogram has been made. Then, at the order, "relax," the patient exhales passively. The inspiratory position is assumed again shortly before the time of opacification of the left chambers of the heart and the aorta, and is held until the instruction, "breathe naturally," is given after the last exposure has been made.

The posteroanterior position is used routinely for visualization of the superior vena cava, the lung roots and the pulmonary circulation.

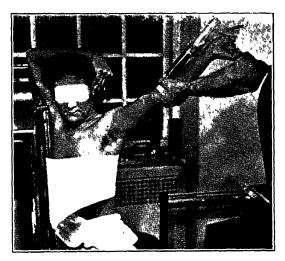


Fig 2—Right anterior oblique position, immediately before injection (viewed from the side) Syringe containing diodrast attached to needle-stopcock unit. Note column of blood above, diodrast and position of injector's hands. (Robb and Steinberg, Am. J. Roentgenol.)

The oblique positions are necessary for study of the heart and thoracic aorta. The left anterior oblique position is used routinely; the right oblique view also is employed when a side view of the heart is desired.

For visualization of the superior vena cava and the right auricle, the time for exposure regularly is $1\frac{1}{2}$ seconds after the beginning of injection. For the right ventricle and the pulmonary arterial tree the interval is usually 3 seconds, but may be 6 seconds or longer if there is

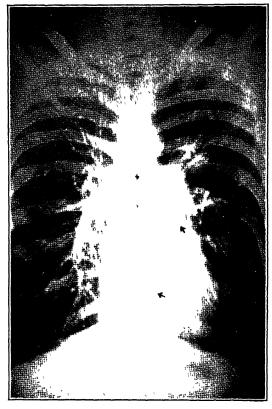


Fig 3—Contrast roentgenogram Three seconds after the beginning of injection Normal, aged 20. The right chambers of the heart, the pulmonic conus, and the entire pulmonary arterial tree are filled with diodrast. The interventricular septum is indicated by the lower arrow, and the left cusp of the pulmonic valve by the upper arrow. The right branch of the pulmonary artery is bracketed by darts (Robb and Steinberg, Am. J. Roentgenol.)

pulmonary emphysema or other cause for slow venous inflow

The time for exposure of the left ventricle generally varies between 6 and 9 seconds with an average of 8, but it may exceed 20 seconds.

Contraindications to the use of diodrast are severe liver disorders, nephritis,

and hyperthyroidism. The test should be used cautiously in patients with heart disease and circulatory failure. It should not be used in patients who are critically Premedication with a barbiturate 111 compound is advisable for nervousness. Epinephrine should be given when there is an allergic tendency or hypertension. The stomach should be empty or nearly so to prevent nausea and vomiting and the solution should be clear and warmed to 99 6° F (37 5° C.). The sensations to be experienced should be described to the patient to allay apprehension before injection and to prevent excitement during the immediate reaction

To date, 48 injections have been made for pharmacological study and 190 for visualization

Immediate reactions appear in 10 to 20 seconds after the injection. They consist of a metallic taste, and a wave of intense heat which starts in the mouth and spreads through the body. Concurrently, there is a fall in arterial blood pressure which rarely exceeds 30 mm. Hg, a rise in heart rate of approximately 30 beats per minute and flushing of the face and the shoulders. Dizziness, weakness and nausea are observed occasionally. Transient pain and venospasm at the site of injection occur in a few instances.

Delayed reactions occurred infrequently Urticaria appeared promptly in 15 patients and angioneurotic edema in 2 others, epinephrine gave prompt relief Dermatitis medicamentosa occurred only once. A slight elevation of temperature was observed 9 times, in 2 other patients, a chill and high fever followed injection Mild thrombophlebitis developed at the site of injection 33 times but was unimportant since it involved only a small segment and caused neither discomfort or embolism. No toxic effect

upon the heart, the lungs, the kidneys, the liver, and blood could be observed.

This method gives exact information regarding the chambers of the heart and pulmonary circulation. A new field for the study of the anatomy and the physiology of the circulation is opened up.

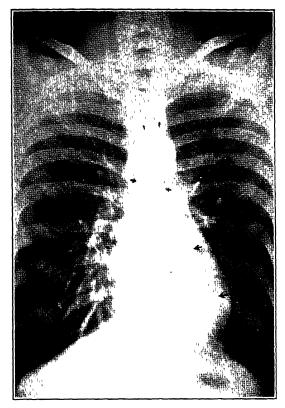


Fig 4—Same patient as in Fig 3 Contrast roentgenogram. Eight seconds after injection. The left auricle and the left ventricle are indicated by the middle and lowest arrows on the left side, a pulmonary vein by the lower right dart. The ascending aorta is enclosed by small arrows. Note the 2 branches from the aortic arch and the left axillary aftery. (Robb and Steinberg. Am J. Roentgenol.)

G P Robb and I Steinberg² report their findings in the 4 common types of cardiovascular disease, namely: Rheumatic; syphilitic, hypertensive, and arteriosclerotic.

In mitral stenosis and insufficiency, the prominence of the pulmonary arc in the frontal view is caused directly by the dilated pulmonary artery and not by the

enlarged pulmonary conus or left atrium. Also elevation of the left bronchus was not caused by the left atrium but apparently by engorged pulmonary veins. In syphilitic aortitis, the most frequent site of involvement, the intracardiac portion of the aorta, was outlined and the exact size, shape and position of aneurisms of the aorta determined. In hypertensive heart disease the exact degree of dilatation and tortuosity of the aorta and buckling of the mominate artery was demonstrated. In the patient with arteriosclerotic cardiovascular disease, the heart was found to be normal in size, the apparent enlargement in the roentgenogram being due to the deviated spine, whereas the aorta exhibited a moderate degree of dilatation, elongation, and unfolding with calcification and thickening of the walls.

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The authors suggest that this method will place conventional roentgenography on a firmer footing, enhancing its clinical value, need for exact visualization of the chambers being reserved for those cases presenting unusually difficult diagnostic problems

ACQUIRED VALVULAR HEART DISEASE

M C. Sosman³ points out that there are 3 important basic facts to remember before considering the individual lesion (1) The roentgenological method is of most value to the clinician when trying to decide if heart disease is present. Cardiac enlargement indicates heart disease, but serious cardiac involvement may be present in a heart with a normal contour (2) The x-ray examination is one of a number of physical examinations (3) Valvular disease of the heart sooner or later results in hypertrophy or dilatation of 1 or more chambers, and causes typ-

ical changes in the cardiac contour in the great majority.

During roentgenoscopy, particular attention should be paid to calcification in the valves, as this has been demonstrated in a great many hearts at necropsy Sosman further points out that it is more difficult to diagnose double lesions than lesions of 1 valve only. Ordinarily, 1 valve will be involved first, and if 1 valve is calcified and the other not, we may infer that the calcified valve was involved primarily.

GALL-BLADDER AND BILIARY TRACT⁴

X-ray Diagnosis — Until 1924 and the discovery of the Graham test, radiology played only a minor rôle in the revelation of biliary affections. Since then, a satisfactory drug for oral administration has been found and accorded general preference over the older intravenous method.

Preparation requires careful attention to details. Kirklin's instructions for a 60-grain (4 Gm) dose of tetraiodophenolphthalem dissolved in 1 ounce (30 cc) of distilled water was quoted "(1) At 6 P M eat supper of usual amount, but without eggs, cream, butter, or other fats (2) Immediately after supper, empty the entire contents of this bottle (the dve) into a glassful of grape juice, stir well and drink it all (3) Do not take a laxative or any other medicine. (4) At 7 o'clock next morning. take a rectal injection of warm salt solution until the water returns clear. (5) Do not eat breakfast; you may drink water, black coffee, or clear tea" Three sets of films are made, 1 at 14 hours, 1 at 16 hours, and a third after the ingestion of a glassful of milk and cream in equal parts following the patient's usual

lunch The films are viewed between exposures and technical corrections made. If this procedure is adhered to, re-examinations will scarcely exceed 5 per cent.

Primarily cholecystography is a test of the ability of the gall-bladder to receive and concentrate dye. This should therefore be mentioned first in the report, and the criteria of a normal response should always be liberal.

Absence of any shadow of dye indicates abnormal function. If the term "faint" is restricted to a shadow so delicate that it is hard to discern, less than 7 per cent of these patients will fail to have disease

Mottling of the shadow with local transradiant or dense areas is indicative of cholecystic tumors or gallstones, although causes outside the gall-bladder must be excluded When the gall-bladder shadow remains the same size throughout the examination, disease is probably present and the patient should be reexamined without dye. Hourglass deformity and certain congenital anomalies, such as reduplications of the gall-bladder, are readily apparent when the viscus is depicted by the dye

The shadow cast by gall-stones will depend on their relative calcium content. Small calculi are often best seen in the third film when the gall-bladder is contracted and the dye partially expelled

Benign papillomas were found in 85 per cent of more than 15,000 gall-bladders surgically removed at the clinic. They are usually less than 05 cm in diameter and never close together. They are most often remote from the fundus.

In contrast to papillomas, adenomas are most often single and situated immediately at the pole of the fundus. They may attain a size of 2 cm.

Carcinoma has a tendency to originate in the neck of the gall-bladder and produce early obstruction, consequently no dye enters the gall-bladder to produce a shadow.

In general, 95 per cent of all chole-cystographic diagnoses should be confirmed at operation. Ninety-eight per cent based on the absence of any dye should be confirmed and 94 per cent of faint shadows should prove significant of disease. Gall-stones should be recognized in 70 per cent and of the remaining 30 per cent, 28 will be diagnosed abnormally functioning gall-bladder. The proportion of papillomas, adenomas, and other benign tumors discovered will not be large.

Although a positive diagnosis is highly accurate, errors up to 10 per cent to discover existing disease are not unusual. Extra biliary disease, such as diabetes mellitus, peptic ulcer, obesity, pernicious anemia, thyrotoxicosis, myxedema, pulmonary tuberculosis, and appendicitis have little or no influence on the cholecystographic response

In conclusion, it should be remembered that a normal response is not fallacious.

RADIOLOGY IN OBSTETRICS

J B Hartley⁵ correlates the information obtained from a routine radiologic examination in pregnancy. The possibilities and limitations are discussed and in numerous instances illustrated by cases and roentgenograms.

The technic should satisfy the following criteria

- 1 It should be generally applicable
- 2 It should bear some relation to the conditions obtaining at the time of delivery
- 3. It should be capable of giving the necessary information for pelvimetry, or should be easily adaptable to give this information as required.
- 4 It should enable an answer to be given, from routine films, to as many obstetrical problems as possible.

- 5. It should be accurate and must not permit, under any circumstances, even if an error of judgment be made, of any information being given which may lead a patient to enter a labor which has no hope of being successful.
- 6 It should be harmless to both mother and fetus
- 7. It should enable comparisons in successive pregnancies in the same individual

Hooton's technic is used and the claim that this is correct to within $\frac{1}{12}$ inch is substantiated by the author.

Detection of the fetus is possible after the sixteenth week but depends on preparation of the patient and careful technic. Nonvisualization does not necessarily rule out a pregnancy. Estimation of fetal age may be based on size of the fetal head and general development of the body

Fetal death is diagnosed by Spalding's sign, which may occur within 64 hours of the death of the fetus. Failure to grow and sagging of the fetal parts is also a sign of death

In the majority of cases, information of an exact nature on the following points may be gained

- 1 Presence or absence of a fetus, number of fetuses.
 - 2 Viability or death of the fetus
- 3 The presenting part, or parts, and then relationship to the pelvic canal
- 4 Shape of the pelvic inlet and outlet, all deformities being exactly demonstrable in size and degree
- 5 Inclination of the pelvic inlet from the horizontal and of the axis of the uterus (anteroposterior or lateral deviation), in relation to the pelvic inlet.
 - 6 Fetal deformities.
 - 7 Hydrammos
 - 8. Pelvic measurements
 - 9 Cephalic measurements

In addition, in expert hands, the following information may be obtained:

- 1 The duration of pregnancy
- 2 Disproportion
- 3 The reason for nondescent of the head at full term.

- 4. Intrauterine or extrauterine pregnancy.
- 5. Postmaturity.
- 6 Pregnancy with abdominal abnormalities.
- W. E. Caldwell, H. C. Moloy and P. C. Swenson⁶ stress the importance of the roentgenologist and obstetrician being trained to appreciate the signifi-
- 1. The presentation of the fetus, fetal abnormalities, the presence of multiple pregnancy, signs of fetal death, etc.
- 2. The size and shape (anatomical classification) of the maternal pelvis
- 3. The size and shape and the degree of flexion or extension of the fetal head.
- 4. Fetal-pelvic relationships, i. e., the obstetrical position of the fetal head with relation to

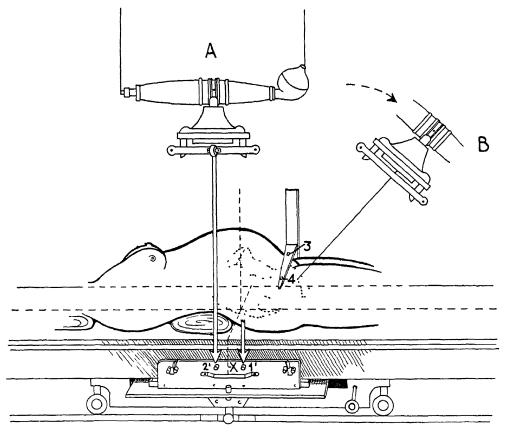


Fig. 5—Stereoroentgenograms. The patient is placed supine with the anterior superior spines perpendicularly above the midpoint, X, of the tube shift. Lumbosacral pad in place. The target placed at a 25-inch tube-film distance is centered for the first exposure over the center of the table and plumbed to peg 2' of the casette frame fixed to the table edge. For the second exposure, the tube is shifted caudad 2'4 inches and plumbed to peg 1' of the casette frame. The known marker (3 and 4) is suspended just tree of the lower abdomen above the symphysis B. The 45° angle view of the subpublic arch. Lumbosacral pad removed. Target is moved downward and tilted at approximately right angles to the public symphysis and rami. (Caldwell, Moloy and Swenson. Am. J. Roentgenol.)

cance of what may be observed in films, particularly those factors in the pelvis and fetal head which cause the common forms of mechanical complications of labor

The following information may be obtained from a roentgenologic examination at or near term:

the pelvic inlet, and the station of the head with relation to the symphysis in front or the sacrum behind

5. The level of the head in respect to the pelvic inlet

From a roentgenological standpoint, the factors concerned in labor may be divided into 2 classes: The measurable; RADIOLOGY 1009

and immeasurable. The measurable consist of the classical pelvic diameters; the immeasurable refer to the shape, position, or relationship of 1 anatomical part to the other. To date the roentgenologist has been concerned primarily with the former, paying little attention to the application of the latter terms to the difficulty or ease of delivery. This study, by determining how the fetal head descends through pelves of various shapes, attempts to demonstrate the fetal and pelvic factors which cause arrest in the occipitoposterior and in the transverse position, and the correct mechanical principles to employ in forceps operations and other related obstetrical problems

Most methods of roentgen pelvimetry and cephalometry are modifications of the so-called frame or position methods and of the parallax, or stereoscopic meth-Pelvis measurements obtained by any one of these methods or their numerous modifications are accurate within practical limits Schumann, for example, by direct measurement of the inlet diameters at operation has shown that Thoms' method of pelvimetry is accurate within 2 mm Clifford has reported favorably upon the accuracy of Johnson's method for the pelvic and fetal head and of the pelvis at the inlet and the ischial spines The results of Ball's work tend to indicate that head volume is a better index of head size than the classical cephalic diameters This method would also seem to be the most practical of those which attempt to estimate ease or difficulty of delivery from head size alone However. estimation of the head volume does not take into consideration the shape of the head. Goodwin has recently drawn attention to the importance of head shape in labor. Two general types may be recognized: The long oval and the round The long narrow type of head usually flexes and moulds well, whereas the round head not infrequently moulds with difficulty. Experience has shown that a primigravida with an average or small child may require operative delivery, while the same patient as a multigravida may deliver easily a larger baby; also serious difficulty may be encountered when no bony disproportion exists. For

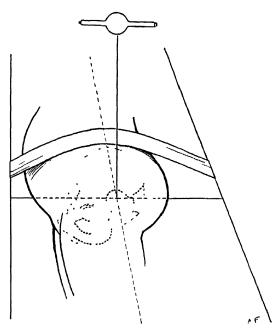


Fig 6—Lateral exposure to outline the sacrosciatic notch. The target is centered over depression just posterior to the greater trochanter of the femur (Target-film distance 36 inches.) (Caldwell, Moloy and Swenson Am. J. Roentgenol.)

these reasons, measurements alone do not answer all of the questions.

The roentgenologic examinations of the pelves of pregnant women used in this study consist of anteroposterior ster-coroentgenograms, a lateral view to include the sacrosciatic notch, sacrum and pubes, and a 45-degree angle view of the subpubic arch. During labor, the view of the subpubic arch may be omitted. The stereoscopic anteroposterior films are viewed and measurements made with the precision stereoscope. Should the observer not feel reasonably sure of his measurements with this method, the

technic described by Ball should be resorted to as a check.

In analyzing pelvic shape and for the purpose of description, the pelvis is divided into the upper pelvis (inlet); the midpelvis (level of the ischial spines); the lower posterior pelvis (the space above the sacrococcygeal platform); and

tion and curvature of the sacrum behind and the inclination of the symphysis and pubic rami in front Transverse diameters from the inlet to the tuberosities of the ischium are influenced by the splay of the side walls of the pelvis, the length of the ischial spines, and the size and shape of the subpubic arch. It must be

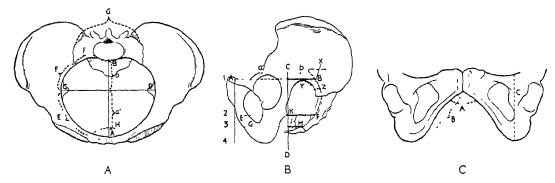


Fig 7—A, analysis of pelvic capacity from the inlet view cd—coronal plane passing through the widest transverse diameter and the ischial spines to form the anterior and posterior segments ab—anteroposterior diameter of inlet and its 2 parts; the anterior and posterior sagittal diameter a' and b' c—anterior puboliac boundary of the anterior segment f—posterior iliac boundary of the posterior segment f'—sacral portion of boundary of posterior segment variable according to width of sacrum, gh—angle of fore pelvis behind symphysis (retropubic angle) variable according to pelvic type

B, analysis of pelvic capacity as viewed from the lateral aspect 1, 2, 3, 4—parallel pelvic planes cd—coronal plane through widest transverse diameter of inlet and the interspinous diameter at right angles to the parallel pelvic planes ab—anteroposterior diameter of inlet with the anterior and posterior sagittal diameters a' and b' y—size and shape of sacrosciatic notch Variable according to pelvic type z—section of ilium which may preserve good length to posterior sagittal diameter (b') in spite of a narrow sacrosciatic notch r—inclination of the sacrum, the of the angle subtended by the plane of the inlet ab and the upper surface of the sacrum kf—posterior sagittal at level of ischial spines gh—anteroposterior diameter of outlet in front of the sacral tip. Note the level of the sacrococcygeal platform to the plane of the spines at f Note length of posterior sagittal at level of third plane (heavy part of line gh)

C, analysis of pelvic capacity front view a—angle of subpubic arch. Variable in size and shape b—variations in curvature of pubic rami. c—depth of true pelvis. (Caldwell, Moloy and Swenson. Am. J. Roentgenol.)

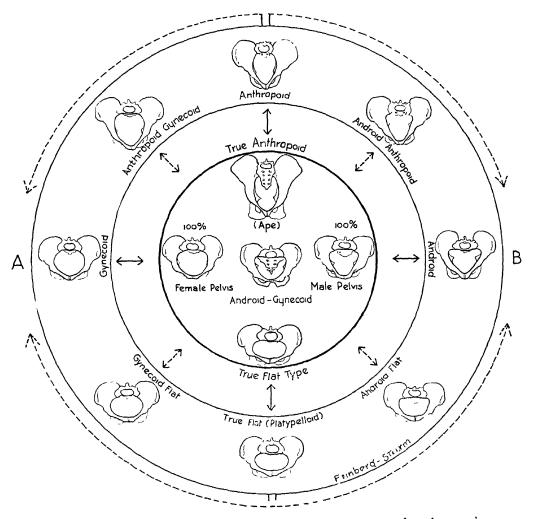
the lower anterior pelvis or outlet (the space in front of the sacral tip). The pelvis is divided into an anterior and posterior segment by a coronal plane passing through the widest transverse diameter of the inlet and through the interspinous diameter. At the inlet, the lengths of the anterior and posterior sagittal diameters and the widest transverse diameter vary according to the basic inlet type. At lower levels, the anterior and posterior sagittal diameters are affected by variations in the inclina-

remembered that the free space of the subpubic arch does not become available for the head until the head is low on the pelvic floor in the fore pelvis

Classification of Pelves—Pelves are classified according to the shape of the inlet in association with a description of the boundaries of the true pelvis at lower levels. Four standard parent or pure types have been selected to form the basis for a simplified morphologic classification and a terminology is proposed which describes these 4 types. By

suitable combination, these terms also describe the shape of the mixed, or borderline forms. The posterior segment of the inlet is formed by the sacrum and a

mixed or borderline forms, the first term used indicates the shape of the posterior segment and the second the shape of the anterior segment.



Factors which affect pelvic form A Evolutionary—transition from long oval (anthropoid) to the flat type (vertical axis) B Sexual—overlap of masculine characters from the gynecoid to extreme android type (trans axis) and within the evolutionary cycle

Fig 8—Diagram to show the gradation of change in pelvic form from a longitudinal oval to a transverse oval, the presence of masculine characteristics and the relation of borderline or mixed forms to the parent 4 types (Caldwell, Moloy and Swenson Am. J. Roentgenol.)

portion of the 2 iliac bones in the region of the sacrosciatic notch. The anterior segment is formed by the ilia along with the publis. Accordingly, the posterior segment may conform to 1 standard type and the anterior to another, producing

- (1) The Anthropoid Type—This pelvis closely resembles the shape of the pelvis of the anthropoid apes and presents a long, narrow, oval shape
- (2) The Gynecoid Type—This type refers to the normal female pelvis, which

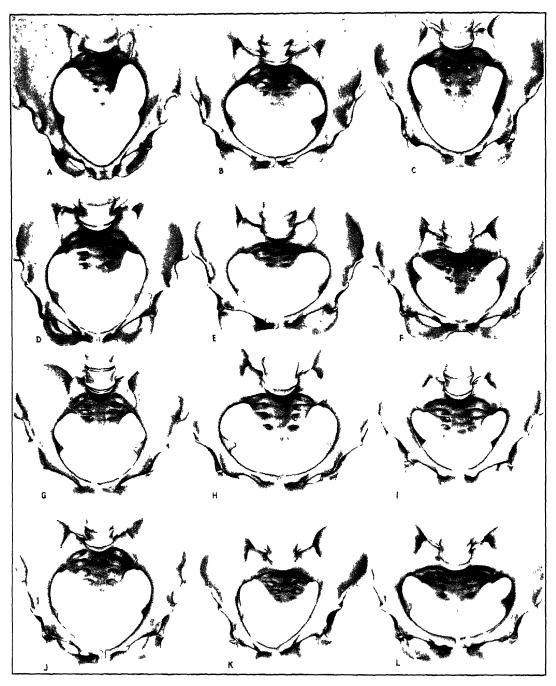


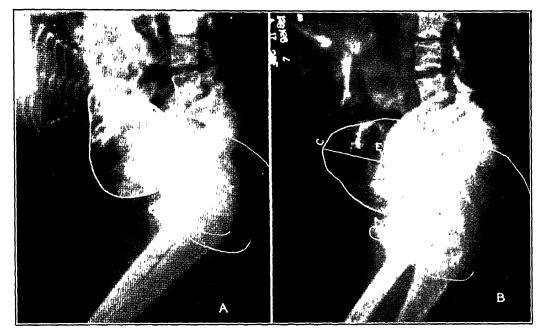
Fig 9—Diagrams of the 4 parent forms and the common borderline types. The examples shown in D, G, and I should all be grouped in the anthropoid-gynecoid class for the sake of simplicity A. True anthropoid type (parent type), B, true gynecoid type (parent type), C, android-anthropoid type (mixed form), D, anthropoid-gynecoid type (mixed form), E, gynecoid-flat type (mixed form) somewhat similar to the 4-sided type of Weber, H, true platypelloid (flat) type (parent type), I, true android type (parent type), I, gynecoid with a narrow fore pelvis (mixed type), K, asymmetrical type, L, android-flat type (mixed form). (Caldwell, Moloy and Swenson Am I Roentgenol)

presents all of the well-known female sex architectural characteristics. The form of the inlet is round.

- (3) The Platypelloid Type—This pelvis is essentially human in characteristics and presents a wide or transverse oval appearance.
- (4) The Android Type—This pelvis bears a morphological resemblance to the

upright sacrum with the symphysis parallel to it, but at a considerably lower level. The sacrum is long and narrow and may contain 6 segments.

In the typical gynecoid pelvis, the ratio between the inlet diameters is approximately 11 to 13. In the extreme gynecoid type, the inlet is well curved and capacious in both segments. The



ling 10—4 Lateral roentgenogram early in labor. Extreme posterior parietal position at inlet. Such a marked degree is lare ab—first plane at inlet and true conjugate diameter cd—long axis of tetal head cf—perpendicular to inlet through midpoint of true conjugate diameter. Note relationship of cd to cf and ab B Lateral roentgenogram early in labor extreme anterior parietal position so rare in this degree as to be considered an obstetrical currosity ab—first plane of inlet and true conjugate diameter cd—long axis of fetal head ef—perpendicular to inlet through midpoint of true conjugate diameter. Note relationship of cd to cf and ab (Caldwell, Moloy and Swenson Am J. Roentgenol)

human male pelvis. The inlet is wedge-shaped or blunt heart-shaped

The typical anthropoid characteristics reveal a long narrow, oval inlet, but the transverse measurements are adequate in spite of the relative narrowing. The posterior iliac portion of the inlet over the shallow but wide sacrosciatic notch is long. The subpubic arch exists as a narrow incisura under the wide heavy symphysis. The lateral view shows the marked pelvic obliquity as well as the

widest transverse diameter is placed considerably in advance of the promontory. The sacrosciatic notch and the posterior iliac portion of the inlet at the apex of the notch are average in size. The sacrum slopes backward, creating a wide sacrosciatic aperture and insuring ample space in the posterior pelvis. The bones are of average thickness. The subpubic arch is wide and smoothly curved. The side walls of the pelvis are straight, preserving down to the intertuberous and

interspinous diameters the transverse capacity present at the inlet.

In the platypelloid pelvis, the anteroposterior diameter is short and the transverse diameter is wide, being placed midway between the symphysis and promontory. The sacrosciatic notch may appear small as a result of foreshortening due to the anteroposterior flattening throughout In addition to the above characteristics, the following regions of the lower pelvis must be described in detail:

- (a) Subpubic arch—Wide, moderate, narrow.
- (b) Pubic rami-straight or curved.
- (c) Splay of the side walls divergent, straight or convergent
- (d) Fore pelvis well formed or funnel-shaped
 - (e) Character of the ischial spines

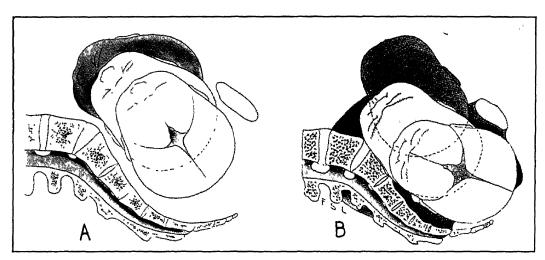


Fig 11—A The common mechanism of engagement and descent as revealed by this investigation. The head engages from a posterior parietal presentation with the sagittal suture of the head pointing toward the symphysis. The anterior parietal bone descends behind the symphysis in a downward and backward direction. B Synchtism Illustrating 1 concept of the mechanism of engagement. This concept assumes that since the symphysis is short and the sacrum is long the posterior aspects of the head must descend more rapidly than the anterior part. This mechanism has not been observed in any roentgenologic examination. (Caldwell, Moloy and Swenson Am. J. Roentgenol.)

the pelvis. The subpubic arch and lower pelvis usually conform to the female type.

The android or male inlet is correctly termed "wedge-shaped". The angle of the fore pelvis at the inlet is narrow. The widest transverse diameter is situated close to the sacrum, and the posterior that portion of the inlet is short. This feature also affects the sacrosciatic notch, which is narrowed. The sacrum is inclined forward approaching the ischial spines. The subpubic arch is narrow, toward which the side walls of the pelvis converge. The bones are heavy and angular, and the true pelvic cavity is deep.

- (f) The sacrosciatic notch—wide, average or masculine type
- (y) The sacrum—general concept of length, width, curvature and number of segments
- (h) Sacral inclination—forward, average or backward
- (1) Lateral bore straight, convergent, or divergent
- (1) Posterior pelvic capacity at the inlet and at the level of the spines and the relation of the sacrococcygeal platform to the latter.
- (k) Shape of the outlet in front of the sacral tip

Finally, the pelvis should be studied as a whole to determine whether it is well formed or angular irrespective of the type.

Pelvic Morphology and Mechanism of Labor—During the past 5 years, a series of approximately 2000 cases have been accumulated from which to study pelvic morphology and the mechanism of

factors warrant consideration: namely, the changes which occur in the direction of the long axis of the head as it is forced and guided in a certain axis through the pelvis and the position of this axis either

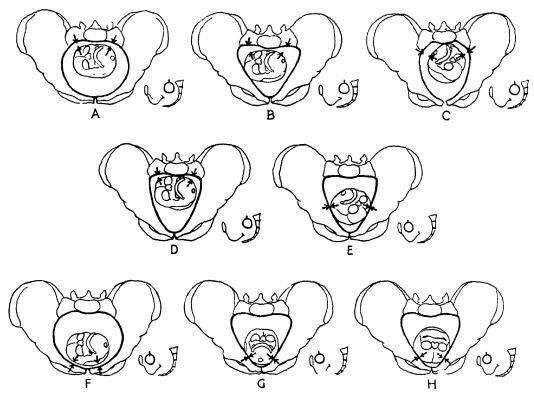


Fig. 12—Adaptation of fetal head to pelvic shape for variable axes of descent. A Transverse position in gynecoid and platypelloid types caused by the shape of the posterior pelvis as the head descends in an axis through the posterior pelvis. B Adaptation of head to transverse position in the android type for the same reason. C Adaptation to the occipitoposterior position or the oblique anterior position in anthropoid type for the same reason. D Adaptation of the head to the transverse position in the android-anthropoid type as head descends through posterior pelvis due to the flat posterior segment. E Adaptation of the head to an occipitoposterior position (or anterior position) as the head descends through axis in the fore pelvis in the android-anthropoid type. F Adaptation of the head to a transverse position with descent through the fore pelvis in pelves possessing a wide angle at the inlet (retropubic angle). G Adaptation of the head to an anterior position in a narrow fore pelvis when the head descends through the anterior segment. As a result of these principles of head adaptation, the obstetrical position of the head after engagement has occurred may be quite different from the position which existed before the onset of labor. (Caldwell, Moloy and Swenson. Am. J. Roentgenol.)

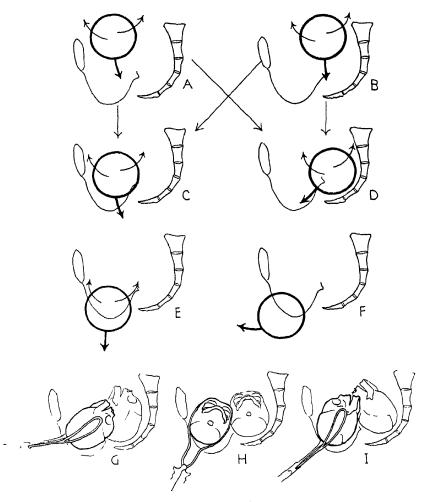
labor, 1000 of these cases were studied during labor itself and from these it has been possible to draw conclusions as to the actual mechanism of labor. Flexion and moulding of the fetal head occur in varying degrees whenever bony or soft-part resistance is met. From the stand-point of fetal-pelvic relationship, 2 other

with relation to the symphysis in front or the sacrum behind

At term, just before the onset of labor, the long axis of the head may show the varying degrees of asynchism or angulation to the inlet illustrated in Fig. 10

The posterior parietal position is known as Litzman's or Varnier's obli-

quity and the anterior parietal position is referred to as Nagele's obliquity. In the majority of instances, engagement begins In normal labor, the stereoroentgenograms show that in the majority of cases the mechanism of engagement and de-



log 13—A diagrammatic attempt to illustrate certain principles to be considered in the use of the obstetrical forceps of in manual methods of assisting labor. It is to be realized that a head in the position illustrated in A may descend downward to C or downward and backward to the position shown in D. The head in B may be carried downward to D or downward and forward to position shown in C. Rotation of the head depends upon the shape of the pelvis at the level of airest or its shape above or below. A head arrested as in A should be deviated downward and backward. A head arrested as in B should be brought downward. A head arrested at C should be deviated downward and backward away from the symphysis. A head arrested at D must be brought downward and forward into the pelvic outlet. A head arrested over the outlet as in E should be brought to a lower level downward before the act of extension as in E. In the diagrams shown in E, E, and E is an attempt has been made to illustrate how forceps should bring a head forward over the outlet from an arrest in the posterior pelvis as in E. The act of extension for arrest in anterior oblique position. E is the posterior positions. The head becomes flexed as the brow meets the resistance of the anterior portions of the fully dilated cervix or the pubic symphysis. (Caldwell, Moloy and Swenson. Am. J. Roentgenol.)

with the head assuming a moderate degree of asynchism and showing a tendency toward a posterior parietal presentation.

scent occurs along an axis in the posterior pelvis. This observation supports the contention that the axis of the lower uterine segment and cervix is commonly RADIOLOGY 1017

maintained in this posterior region by its fascial supports. For this reason, the head is made to descend in the most ample part of the pelvic cavity, the posterior segment. At the bottom of the posterior pelvis, anterior rotation from the occipitoposterior or transverse position begins and is completed when the head is forced downward and forward to a lower level in the outlet itself. In contrast to descent through the posterior segment, labor is usually prolonged and asosciated with uterine inertia and slow dilatation of the cervix in the anterior segment.

The axis of descent may be explained for a round or oval head in the 4 parent types of pelves previously described

For gynecoid, platypelloid, and android types, the flat straight margin of the sacrum predisposes to a transverse position of the head if it is brought close enough to the sacral region. In the anthropoid types, the transversely narrowed inlet, in association with the sacral concavity, more easily admits the head in anterior or posterior oblique positions. The borderline types are described in the preceding illustration.

Knowledge of the axis of descent and the rôle of pelvic shape in determining the obstetrical position of the head is important in the management of labor and in the treatment of pelvic arrest. As soon as the roentgenologist has obtained sufficient experience in film interpretation to appreciate pelvic type and the fetal-pelvic relationships during labor, practical suggestions may be offered with regard to the axis of traction, the proper level for the anterior rotation of the head and the optimum mechanism through the lower pelvis During the past 18 months the attending and resident staff of the Sloan Hospital for Women have made a definite attempt to apply this The result has been a deinformation

crease in the incidence of difficult forceps deliveries by means of more careful selection of cases for cesarian section, yet the incidence of the latter operation has not increased. Forceps operations have been handled on better mechanical principles and with a decrease in fetal mortality because there has been a more accurate knowledge of the shape of the pelvis and of the position of the head Although by a study of the roentgenograms taken before labor, it may be possible to predict the type of labor which will ensue in certain cases, the many factors involved make the films taken during labor more valuable.

ALLERGIC REACTIONS TO CONTRAST INJECTIONS FOR UROGRAPHY

K A. Hultborn⁷ reports 7 cases of complications in urographic contrast media injections and adds these to 8 similar cases found in the literature. One of the latter was fatal. The symptoms were interpreted as allergic reactions released by the dye. The author recommends taking an allergic history before injection and proceeding very cautiously if a positive history is found. For complications, he recommends calcium intravenously and adrenalin subcutaneously. For shock he recommends analeptics and, if necessary, intravenous drip

ROENTGEN EXAMINATION OF THE COLON

J. C. Root⁸ illustrates the value of this method of diagnosis in visualizing anomalies, functional disorders, and organic lesions.

Anomalies, while of little or no clinical significance, are of interest. Probably the commonest is variation in

length of the color and next, variation in position. The cecum due to 3 variations in development may be found in almost any part of the abdomen except the left upper quadrant Failure of rotation allows the cecum to he at any location from the liver to the right iliac fossa. A long mesocecum allows a wide



Fig 14 — Diverticulosis of the sigmoid colon. These small, protruding sacs represent the characteristic appearance of the herniation of the intestinal mucosa through the intestinal wall. (Root S. Clin. North America, W. B. Saunders Co.)

range of mobility and lastly the relatively rare anomaly of complete transposition of the viscera may occur. If an anomalous position is demonstrated before operation, the surgeon may better plan his approach

Functional disorders are usually of an atomic or spastic nature with the latter predominating. In an affonic bowel, the diameter is increased and the haustral markings are shallow and ill-defined. This type of colon usually empties poorly.

A spastic colon may produce various symptoms from mild cramps to severe pain simulating peptic ulcer or cholecystitis. While the barium is being given the lumen may fill rapidly, the diameter appear narrowed, and the patient may

experience distress similar to his usual complaints. A small, spastic left colon with a dilated right colon is characteristic of long continued, intermittent, partial obstruction.

Spastic colon may be secondary to organic disease elsewhere. If a local area of spasticity persists, it may be well to administer antispasmodics and repeat the examination in order to rule out organic disease.

Of all organic lesions, diverticulosis is the commonest, being present in 7 per cent of all colon studies at the Cleveland Clinic.

These are usually hernations of the mucosa through the muscular coat and occur most frequently where the blood vessels pierce the wall. They are increasingly frequent as the age group advances. They are seen to better advantage in the



Fig 15—Irradiation stricture Nariowing of the lumen and partial obstruction due to previous radium treatment of carcinoma of the uterine ceivix (Root S Clin North America, W B Saunders Co)

film following evacuation. In spite of their thin walls, rupture is uncommon

Diverticula alone produce no symptoms. When inflammation is added as a complicating factor, it may produce pain of varying degrees and in some

cases there may be intestinal obstruction. In the latter condition, carcinoma must be differentiated. Diverticulitis usually involves a long segment and is tender and immobile to palpation. Cancer usually shows better defined borders, is not tender and in the early stages is not fixed. The absence of x-ray evidence of diverticula does not exclude a diagnosis



Fig 16—Chronic, nonspecific ulcerative colitis. The involvement here is of the rectum and distal sigmoid colon. Note the contracted rectum and smooth nonhaustrated contour of the involved bowel. (Root. S. Clin. North. America, W. B. Saunders, Co.)

of diverticulitis as inflammatory changes and fecal material may occlude the lumen

Benign stricture following irradiation of the uterus for cancer must be differentiated from an extension of the neoplastic process

Differentiation from a roentgenological standpoint alone may be impossible but a history of previous maddation may help clear up the problem

An early roentgen diagnosis of ulcerative colitis may be impossible even though a positive diagnosis has been made by proctoscopic examination. As the disease progresses, straight, rigid walls due to infiltration together with shortening of the bowel become apparent. The haustra are absent and in the film following evacuation the normal mucosal markings are absent.

Ulcerative colitis is commonest in early and middle adult life but may appear in



Fig 17—Chronic, nonspecific ulcerative colitis, regional type Note the marked contraction and smooth wall of the transverse colon The large bowel both proximal and distal to this segment is normal (Root S Clin North America, W B Saunders Co)



Fig 18—Ulcerative tuberculosis Spastic defect in the cecum and small lumen of terminal ileum due to tuberculous lesion (Root S Clin North America, W B Saunders Co)

any age group. In 95 per cent the lesion appears in the rectum and spreads by continuity to the cecum. In the remaining 5 per cent, any location or multiple

loci with normal intervening mucosa may be present.

In the long standing cases, polypoid changes may appear. These also may be localized or diffuse.



Fig 19—Hyperplastic tuberculosis Filling defects in cecum produced by tuberculous process Note resemblance to filling defect due to cancer (Root S. Clin North America, W. B. Saunders Co.)



Fig 20—Adenocarcinoma Extensive, irregular filling defect in the ascending colon (Root S Clin North America, W B Saunders Co)

Amebiasis may produce similar roentgenologic findings in the right colon, but these are unusual as one more often finds no change in the colon in this disease. Under polypoid lesions are grouped all organic lesions, benign or malignant which protrude into the bowel. A double contrast enema must be employed in addition to the usual films, as small lesions may be overlooked unless this is done.

Multiple small polyps may involve the entire colon or only a portion. The inci-



Fig 21—Adenocarcinoma of the sigmoid colon Note the small lumen and filling defect in the proximal end of the dilated distal sigmoid (Root S Clin North America, W. B Saunders Co)

dence of malignancy in polypoid lesions will roughly be in direct ratio to the number of polyps present

Tuberculosis of the gastrointestinal tract is a frequent complication of open, advanced pulmonary lesions. The usual site of involvement is the ileocecal region. Primary tuberculosis of the colon is rare but when it does occur, it is usually of the hyperplastic type.

The ulcerative type of lesion is commoner and manifests itself during roentgen examination as a spastic filling defect

Tuberculosis is usually found in young individuals, whereas carcinoma is commoner in patients past middle life. A film showing open pulmonary tuberculosis is of great aid.

Carcinoma is characterized primarily by definite and permanent filling defects with marked destruction and alteration in the mucosal pattern. While variations in size and contour may be produced, the growth will always be found to be adenocarcinoma, even though in some sites it appears to be quite smooth and resembles a scirrhous lesion.

As the size of the lumen decreases toward the terminal end and the contents become more solid, the growth produces an obstructing lesion proportionately earlier in the disease. Here, too, the lesion may be smaller and produce a typical "napkin ring" appearance. The ends of the lesion are well defined and the proximal bowel is dilated. Carcinoma is primarily a lesion of the mucosa and hence will produce the majority of changes in the mucosa itself.

Sarcoma of the bowel occurs rarely Roentgenologically, it cannot be differentiated from carcinoma. Since the sarcoma starts in the submucosa, the mucosal pattern is usually altered to a less extent. A sarcoma as a rule responds to roentgen therapy, a point that will assist in the diagnosis if operation is not feasible.

ASCARIASIS

Roentgen Diagnosis -- \ Barbieri⁹ states that the easiest way to diagnose ascariasis roentgenologically is by means of an opaque substance. The parasites are demonstrated by filling defects. Their presence may be suggested by multiple fluid levels, and, therefore, films in the erect posture should never be neglected. In examining the lower part of the small intestines pressure may be necessary to separate the superimposed loops, and repeated observation is necessary.

The commonest aspect is a streaky filling defect with parallel borders, in

the vicinity of which the barum shadow assumes a gradual haziness which increases toward the axis of the body to give an impression of roundness. The width of the image varies from 3 to 8 mm.

When the digestive tube of the worm is filled with barium, it appears as an opaque streak from 2 to 3 mm. thick and from 10 to 15 cm long, or as an opaque point in the center of a disclike filling defect. This is most frequently observed after the patient has evacuated the opaque meal

Gas may also be used as a contrast medium to outline the ascarides, but when their presence is suspected, roentgen examination with an opaque substance should never be neglected.

RADIUM AND X-RAYS IN THERAPY

Rational Radiotherapy

G. W. Grier¹⁰ states that the fundamental principle of treatment "that it is only necessary to know the amount of radiation to destroy the involved tissues and to apply that dosage where it is needed, protecting surrounding normal tissues" was discovered in the early days of radiation therapy. There has been no fundamental alteration or addition since. In skin lesions, such a method of application is practicable. In deeper lesions, tissue absorption and the fact that the intensity varies inversely as the square of the distance (the inverse square law) are unfavorable Therefore, the treatment of superficial and deep lesions are separate problems.

The lethal dose for most deep-seated cancers varies little from that for the surrounding normal tissue. In treating superficial cancer, the destruction of a few normal cells is not as important.

The amount of radiation required to produce destruction of cancerous cells may also produce sloughing of normal tissues. If the dose is divided, the effect may be more favorable since normal tissues may recover more readily than do malignant cells. This variation in recovery enables one to increase the total depth dose by dividing and fractionating the treatment. However, if the initial or subsequent doses are too small or too far apart, the tissues develop a resistance which defeats the purpose. Therefore, the method of application is as important as the total dose delivered.

Although therapy technic has advanced greatly, one should be careful about standardizing the method and dosage since different locations respond differently, and individuals vary in their response

Radiation Therapy of Cancer

In a discussion of the treatment of cancer by irradiation, G. T. Pack11 states that surgery, the actual cautery and chemical cauterizing agents all have their place in removing or destroying cancerous tissues Radiation therapy, by x-rays and gamma rays from radium, has definite advantages over these other methods in cases of cancer, in which the cancer cells are more easily killed than are the cells of the normal surrounding tissues Radiosensitivity seems to have some relationship to the origin of the cells making up Tumors developing from the cancer primitive blood-forming tissues are likely to be radiosensitive, as, for example, lymphosarcoma, myeloma, endothelioma, and angioma Tumors developing from neural crest cells are likely to be radioresistant, as, for example, glioma, neurosarcoma, melanoma, and mixed tumor of the parotid

Methods of Radiation Therapy— Irradiation therapy may be applied by 2 methods: (1) From an external source; (2) from a source applied directly into the tumor or surrounding it.

External radiation may be given by x-rays with low voltage for superficial lesions and with high voltage or supervoltage for deeply seated lesions Radium may be used instead of x-rays for the treatment of superficial lesions by means of small plaques, trays, or moulages. Radium may be used for deeply seated lesions (teleradium therapy) by means of large quantities of radium in bombs or packs several centimeters away from the lesions under treatment.

Intracavitary Irradiation—Radium element in tubes, covered with sufficient platinum, gold, brass, or aluminum for filtration, may be placed within body cavities for contact treatment of cancers of nares, orbits, antra, larynx, esophagus, uterus, or vagina.

Interstitial Irradiation—Radium needles and radon seeds may be driven directly into or placed in groups surrounding cancers in soft tissues. This method of treating accessible tumors is usually supplementary to external irradiation

Units of Dosage—Pack has summed up the subject of dosage used in irradiation therapy concisely in the following words "It is best to administer to all the neoplastic territory, the maximal quantity of radiant energy compatible with the maintenance of tissue integrity To speak intelligently of these quantities it is best to have some common physical and biological measures of the dosage Thus in the case of radium the quantity of gamma rays at the source is known as the 'dose of emission' One knows with precision the dose of emission because this is invariable. The dose emitted is expressed by 2 different notations. The one has for its basis the intensity of the gamma rays and the duration of their RADIOLOGY 1023

application; the intensity is proportional to the quantity of radium present; the dose is obtained by the product of the quantity and the time, which is expressed as milligram hours of radium or as millicurie-hours of radon (gram-hours or curie-hours in the case of large radium bombs or packs). The other notation, which is utilized throughout France, makes the dose proportional to the quantity of radium emanation destroyed (disintegrated) during the course of its application This is expressed in terms of 'millicuries-destroyed' or of "microcuries-destroyed,' the latter term connoting only one-thousandth of the former. The physical efficiency of 1 millicurie of radon throughout its life is equivalent to 133 millicurie-hours Therefore, 1 millicuriedestroyed is equivalent to 133 millicuriehours or 133 milligram hours.

"The dose of gamma or roentgen rays at the surface or the point of entrance into the body is the superficial dose while the dose to the tumor by unit volume of the tissues treated is the 'tissue or tumor dose'

"The unit of x-ray dosage called the 'roentgen' or r (designated always by small r) has been standardized and internationally accepted. The roentgen has been defined as that quantity of roentgen radiation which, when the wall effect of the ionization chamber is avoided and the secondary electrons are fully utilized, produces in 1 cubic centimeter of atmospheric air at 0°C and 76 cm mercury pressure such a degree of conductivity by ionization that 1 electrostatic unit of charge is measured at saturation current

"In the measurement of roentgen rays and gamma rays by biological means, the commonest unit is the establishment of an erythema dose under certain conditions Quimby, of the Physics Department of the Memorial Hospital, has de-

fined and employed the term, 'threshold erythema,' which is that dose of radiation that will cause a perceptible change in the skin of 80 per cent of the subjects and no discernible discoloration in 20 per cent in 2 to 4 weeks after exposure to the rays. Quimby has found that the threshold erythema with 200 kv. 100 sq cm field, 50 cm target-skin distance, and filter of 0.5 mm copper and 2.5 mm. aluminum is 500 to 525 roentgens. The therapeutic erythema, on the other hand, varies with different radiologists from 600 to 1000 roentgens."

The Tissue Dose—Cancericidal Dose—At the Memorial Hospital, the "threshold erythema" is used as the unit of tissue dosage. As mentioned above, this can be determined for each x-ray tube and each radium applicator by direct experiment.

At various depths below the surface of the tissue being irradiated, the depth doses can be calculated as being various percentages of the dosage of the radiation falling on the surface. The method of determining these percentages is by making measurements with a small ionization chamber placed first on the surface of a vessel of water and then placed successively at various depths below the surface of the water Such water phantom measurements agree fairly well with measurements obtained by placing the ionization chamber similar distances beneath the surface in various cavities in the human body The data obtained by these water phantom measurements are plotted as "isodose curves" These isodose curves are used for rapid calculation of the depth dosage given to a tumor when irradiated by cross-firing through several portals

In the case of interstitial irradiation, the measurement by direct experiment is more complicated especially as the irradiation is applied from numerous sources

simultaneously. At Memorial Hospital, this has been worked out in a practical manner by Martin and Quimby. They have demonstrated that in any sphere it makes little difference in the dosage at the periphery whether the source of radiation be concentrated at the center or be distributed uniformly within the inner half of the sphere. They have prepared tables for spheres of various sizes giving threshold erythema dosage at the periphery when various quantities of radon are placed near the center or at least within the inner half of the spheres.

The cancericidal doses for many different kinds of tumors have been determined by actual clinical observation and can be stated in terms of threshold erythema dose (T. E. D.) For example, intraoral squamous cell carcinoma requires 6 to 8 T. E. D., while transitional cell carcinoma requires 2 to 4 T. E. D. for sterilization. By calculating external irradiation and interstitial irradiation in terms of the same unit it is convenient then to determine combined external and interstitial irradiation by adding the number of units applied in the 2 methods

Prescription for Roentgen Therapy—For the safety of the patient roentgen-ray dosage must be prescribed in an accurate way and a detailed record should be kept of the treatment given The quantitative factor should be expressed in r units and the qualitative factor in Angstrom units or by stating the half value layer in millimeters of copper, aluminum, or other metallic filters In addition to these 2 factors should be specified the kilovoltage, filtration, target-skin distance, and time of application in minutes. The tumor depth below the surface should usually be indicated The size and number of the portals through which treatments are given are also important as is also the factor of number of treatments and

the intervals between treatments. A single massive dose has an effect quite different from that of the same total dosage fractionated over several weeks or months.

Kilovoltage (Potential) — As the voltage or potential applied to the x-ray tube is increased the average wave length of the rays emitted becomes shorter Short waves penetrate tissues more readily than longer waves. This important factor is utilized in therapy of tumors deep below the surface by applying high voltages of 200 kv. to 1000 kv. For therapy of superficial skin diseases, lower voltages are used All x-ray tubes give off rays varying considerably in wave length When the effect of short waves on deep tumors is desired, filters of copper, aluminum, or other metals are employed to absorb the long waves which would have an undesirable effect on the skin and superficial tissues.

Comparison of Teleradium Therapy with Supervoltage Roentgen Therapy—It has been estimated that supervoltages of over 1500 kv. would produce x-rays having wave lengths comparable to the gamma rays of radium. Already there are several 1000 kv. or million-volt machines in use in the United States. The roentgen rays produced by these machines have biological effects differing little, if any, from the effects which follow teleradium therapy with packs containing 4 grams of radium. The roentgen rays have far greater intensity and so can be used to treat more patients in a given time. This greater intensity may not be desirable, however, for therapy spread out over a longer period seems to have advantages

Ionization in Tissues—The destruction of living cells by radiation is due to the release of electrons from the atoms, of which the cells are composed, when these atoms are bombarded by gamma rays or roentgen rays. Finally, the atoms, minus 1 or more electrons, combine with other electrons In some cases the recombination is harmless to the cell but in other cases the recombination is a form of chemical change which brings about the death of the cell.

Current (Milliamperage)—The kilovoltage applied to the terminals of the x-ray tube determines the speed with which the electrons fly across the tube and strike the anode and determines the wave length of the x-rays emitted. In a similar manner, the milliamperage is an indicator of the number of electrons flying across the tube The more electrons flying across the tube, the more x-rays are emitted from the anode in a given length of time. Pack states this concisely in the following words: "The usual roentgen tubes carry from 4 to 30 milliamperes. Thus a tube running at 4 milliamperes for 25 minutes would deliver 100 milliampere-minutes and a tube running at 25 milliamperes for 4 minutes would also deliver 100 milliampere-minutes or its equivalent in roentgens, other conditions remaining the same"

Filter—As previously mentioned, high frequency roentgen rays which have short wave lengths penetrate more deeply into body tissues before their energy is expended than do roentgen rays of lower initial frequency and correspondingly longer wave lengths Conversely, low frequency roentgen rays, which have long wave lengths, expend their energy on the skin or superficial tissues and do not penetrate to the deep tissues When tumors far beneath the surface are to be treated it is necessary to interpose filters of copper, aluminum, or other metals to absorb the rays of long wave length and thus protect the skin and superficial tis-The waves of short wave length pass through copper and other metals if the filter is comparatively thin The number of millimeters of copper or other metal which will cut down the intensity of an x-ray beam to one-half of its initial intensity is called the "half-value layer." It is an indicator of the quality or wave length of the beam. Another way of expressing the effective wave length of the beam is to give the measurement in Angstrom units. The author gives the following data to illustrate:

"Failla and Quimby have found that the effective wave length employed in the usual deep roentgen therapy at the Memorial Hospital is about 0.16 Å. This treatment is given with 200,000 volts (peak), filtered by 0.5 mm Cu and 1 mm Al With intermediate voltage of 140 kv the filter may vary from nothing up to 6 mm of aluminum, with a filter of 4 mm Al the effective wave length is about 0.25 Å

"In the case of radium, the filters employed, brass, lead, silver, gold, or platinum are usually expressed in the equivalents of certain thicknesses of platinum. One millimeter of platinum or its equivalent (occasionally 0.5 mm platinum) is the customary filter for surface application of radium or teleradium therapy. Intracavitary radium treatments are given with filters of 05 to 1 mm of platinum, while interstitial irradiation requires considerably less filtration Gold radon seeds have a wall thickness of 0.3 mm gold and most platinum needles for interstitial use are designed with a wall thickness equivalent to 0.5 mm"

Size of the Field of Irradiation—When roentgen rays and gamma rays strike the human body, a portion of their energy is absorbed by the atoms of which the tissues are composed and rays of longer wave length are given off in various directions. These oblique rays in turn strike other atoms and are given off again in various directions and at still longer wave lengths. After these second-

ary rays have struck many atoms successively, the rays have been scattered in all directions and many of them are even going in the opposite direction from that of the initial rays. In this manner, the skin and superficial tissues are bombarded in all directions by the initial rays plus the scattered secondary rays. It is quite easy to picture this mentally and to comprehend that the larger the area treated by irradiation, the more the scattered rays from portions of the initial beam will overlap the scattered rays from other portions of the beam. The scattered rays may amount to as much as 40 per cent of the total radiation in the skin and superficial tissues. At a depth of 10 cm, the scattered radiation may amount to 80 per cent if the area treated is large This is a very important fact to be considered in planning deep therapy. Large concentration of radiation in deep tumor tissues may be obtained and at the same time skin dosage kept within the limits of toleration, by using small portals and directing the beam accurately at the tumor from several different directions

Target-skin or Radium-skin Distance—Pack has presented the distance factor so concisely that it is quoted.

"The inverse square law of radiation states that the intensity of a beam of roentgen rays or gamma rays varies inversely proportional as the square of the focal-skin distance from a point source Thus the radiation intensity from a high voltage roentgen tube at 50 cm distance is almost twice that delivered at 70 cm focal-skin distance, or a radium applicator placed at 2 cm, radium-skin distance conceivable would deliver 4 times the superficial dose as the same applicator applied for the same time at twice the distance, or 4 cm (This is not exactly true since the radium applicator is not a point source) This fact may be ex-

pressed also in the following manner. Since the dose is dependent on the product of the intensity times the duration of exposure, the radium treatment at 4 cm distance would require 4 times as many minutes or hours as at 2 cm. radium-skin distance. The question naturally arises -why not decrease the focal-skin distance as much as possible to save time and expense? In the case of very superficial noninfiltrating skin cancers, this plan is feasible but for the more deeply situated cancers the depth or tissue dose is increased (in comparison to the dose delivered to the superjacent skin and tissues) with the greater skin-target distance Theoretically, the distance might be increased sufficiently so that the relative dose on the skin at the portal of entry of the rays would be almost the same as at the location of the tumor within the body"

Heublein Method of Continuous Irradiation—The theoretical increase of target-skin distance that the tumor dose and skin dose will be almost the same has been put to experimental trial by Heublein and Craver at the Memorial Hospital The x-ray tube was placed 24 feet away from patients lying in bed. The tube was operated at 185 kv and 3 Ma. The time required to deliver 225 r at 24 feet was 250 hours or 125 days at 20 hours a day. The clinical skin erythema dose of 750 r (measured in air) was the unit of dosage employed.

One hundred and thirty-four cases were treated in 2 years. These were mostly generalized and radiosensitive tumor processes, such as the leukemias, lymphosarcoma, Hodgkin's disease, and multiple myeloma. The results in the treatment of chronic lymphatic leukemias and pseudoleukemia seemed superior to any obtained previously by local irradiation. The treatments were given cautiously at first and dosages were even-

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tually increased to 375 r to 450 r There were no complications resulting from the irradiation except the occasional development of leukopenia, anemia, and thrombocytopenia. This is considered to be one of the most important achievements in radiation therapy in the last decade. Its principles of low intensity, great distance, continuous irradiation, and long duration of treatment may be found of value in the therapy of many cancers which have been refractory to other methods.

The Time-intensity Factor-Satisfactory irradiation treatment in the cure of any cancerous condition involves the adjustment of dosage so that the cancer cells will be destroyed and the normal tissue cells will be allowed to live. It might involve the prevention of reproduction of the cancer cells and allow reproduction of the normal cells In the latter case, the cancer cells would simply die of old age, leaving the succeeding generations of normal cells in undisturbed occupancy The dosage which can be used in therapy is limited by the amount of radiation which the normal cells can receive and still continue to reproduce Regaud, Coutard and Lacassagne performed some very important experiments which allowed them to draw conclusions regarding the method of irradiation which would kill cancer cells and allow the survival of normal tissue Their test materials were rabbits in which various dosages of x-rays were administered to the testicles and anorectal skin and mucosa The rapidly developing spermatogonia resembled in many ways the rapidly developing cancer cells. The skin and mucous membrane were representative of normal tissue cells It was found that the spermatogonia could not be killed by a single massive dose of x-rays without at the same time causing serious damage to the skin and

mucous membrane. When the x-ray treatment was given in several fractional doses with a considerable interval of time between the doses, there was a great difference in effect; the spermatogonia were affected even more than by the single dose, while the skin and mucous membranes were affected less than by a single large dose. Pack states this in the following manner:

"Regaud's explanation of the superiority of continuous or fractionated irradiation over short intensive treatments is founded on the existence of alternating periods of radiosensitivity and of radioresistance in the life of the spermatogonia (in the experiments) and the cancer cells (in clinical practice). Spermatogenesis in a mammal such as the rabbit is a continuous phenomenon if the testicle is considered as a whole. But if one considers only a certain cell or line of cells on a seminiferous tubule, the function of reproduction by cell division is seen to be discontinuous and cyclic and the spermatogonialike cancer cells, pass through alternating phases of multiplication (brief phases) and of rest (long phases) In 1 line of cells, either spermatogonia or cancer cells, the phase of multiplication corresponds to accentuation of radiosensitivity (law of Bergonie and Tribondeau), while the phase of rest corresponds to the diminution in radiosensitivity. A short treatment therefore might destroy only those spermatogonia or cancer cells which are dividing at that time, it spares the others. It is only natural that prolonged and continuous irradiation (in the case of radium) or well-fractionated irradiation with proper spacing of the fractions into a fairly long time (in the case of roentgen rays) is more efficient than brief intensive irradiation, because in the first case the germinal or cancer cells are killed one after the other as the cycle progresses and

these cells enter for the moment the phase of maximal radiosensitivity. These principles are now so generally recognized that the prolonged irradiation of low intensity or fractionated cumulative treatments have found almost universal favor with roentgenologists and radium therapists. These treatments depend usually on the administration of suberythema doses repeated every 24 or 48 hours until a total dose of 6 to 8 threshold erythema units may be delivered to 1 skin portal with perfect safety. To illustrate the application of this principle, let us consider the treatment of a hypopharyngeal carcinoma by high voltage roentgen rays only Two lateral portals are used to cross-fire the beams of radiation With a single massive dose, only 850 r can be given to each side of the neck without seriously damaging the skin By the fractionated method, 300 r may be given daily alternating on each side of the neck until a total of 3000 to 4000 r are delivered through each portal. Such a course of treatment requires 3 weeks to consummate the dose required to sterilize the carcinoma."

Summary of Methods of Treatment—There are 4 methods of treatment commonly employed (1) The massive dose technic, (2) saturation dose; (3) fractionated dose, (4) continuous irradiation.

The single massive dose was formerly used and was intended to destroy all the cancer cells at once. If, however, a few cancer cells survived, the cancer might grow again. If the dosage was just below the tolerance of normal tissue cells the skin and superficial tissues would survive. A massive dose treatment could not be repeated for several weeks.

Kingery introduced the saturation dose method in the treatment of skin diseases by low voltage x-rays without any filter. He gave an initial erythema

dose and then maintained the biological effect by adding smaller doses at proper intervals. He added 50 per cent of an erythema dose after $3\frac{1}{2}$ days to make up for the recuperation of the tissues from the initial dosage. Pfahler was the first radiologist to use this method in the treatment of cancer by properly filtered high voltage x-rays.

In the fractionated dose method daily treatments are given with doses below an erythema dose. A cumulative effect is obtained. The cancer cells do not recuperate as quickly as normal cells from irradiation and so a cancericidal cumulative dose is reached before a cumulative dose lethal to normal tissue cells is reached. As mentioned previously the irradiation given in repeated dosage is more likely to destroy the rapidly multiplying cancer cells during their periods of cell division.

The continuous method of irradiation, as used by Heublem and Craver with their teleroentgen equipment, is a further development of the method of fractionated small dosages. Treatment is given for 20 hours a day for several weeks with x-ray tubes 24 feet away from the patients

Anti-Inflammatory Roentgenotherapy

Results—R Mathey-Cornat¹² reviews and evaluates the results found in the numerous articles by Freund, Wintz, Gajzago, Spitzenberger, Schwarz, Windbolz and Frank.

Among the inflammatory conditions for which irradiation had been used were such skin affections as furuncles, anthrax, botryomycoma, pyodermitis, ulcers, periphlebitis and cutaneous mammary abscess. Among the stomatological conditions treated were maxillary osteoperiostitis, cervical phlegmon, adenitis, and adenophlegmon. Among the oto-

rhinolaryngological conditions were tonsillitis, tonsillar abscess, pharyngeal abscess and fistula; as well as some cases of sinusitis and mastoid sequelae. Also in certain rheumatoid and virus infections including radiculitis; sciatica, neuritis, lumbago, torticollis and painful arthritis and in some cases of essential epilepsy, arachnoiditis and meningitis in children, good results were obtained.

In the cutaneous disorders results were encouraging but not constant and therefore, in this group, irradiation should only be used as an adjunct to other forms of treatment.

In tonsillitis roentgen therapy yielded many failures and incomplete cures despite doses of from 600 to 800 r. The failures are usually found in simple hypertrophy or sclerosis of the tonsils. In acute or subacute tonsillitis with or without crypts, in peritonsillitis and ir peritonsillar abscess a rapid resorption or early localization which permits incision and drainage may follow.

Good results have been obtained in osteoperiostitis and chronic or subacute phlegmons of the floor of the mouth and submaxillary carotid regions as well as in adentis. Remarkable results were obtained in some cases of parotitis and surgery was not necessary. Dental premaxillary and premandibular swellings have often responded favorably. Surgery may be required later.

Good results have been observed in gynecological roentgenotherapy, both specific and nonspecific. In young individuals the chances of temporary castration should be kept in mind as this may occur from 1 treatment of 20 to 30 per cent of the erythema dose of 600 r. For this reason other forms of treatment should be tried first.

The best results from roentgenotherapy in tuberculous imflammatory process is obtained in the subacute form when the temperature is affected by the menses and intestinal lesions are absent and the lesions located predominantly in the adnexa. The author believes the principal result is from the resulting ovarian castration. The technic and mode of action of roentgenotherapy in all of these conditions is discussed at length.

Acute Pneumonias

Roentgen Treatment - During the past decade so much has been written on the use of roentgen rays in the treatment of acute infectious and inflammatory conditions, especially furuncles, carbuncles and erysipelas, that it is surprising to find so little mention made of roentgen therapy of acute pneumonias There are many references to the use of roentgen therapy for chronic or unresolved pneumonia, but when E Powell¹³ began treating the acute cases 5 years ago, he found no reference giving any specific data as to dosage, results to be expected, or influence, if any, on mortality

In 1933 the author began to use roentgen therapy in alternate cases of acute pneumonia He and the other staff doctors continued to use all other methods of treatment, the same as previously, so that the controls and the x-ray-treated cases received equal treatment, except the irradiation. At that time no antipneumococcic serum was used. It was soon noted that the patients who received the roentgen therapy developed prompt crises in many cases Nearly all of them were relieved of their distress and discomfort within a few hours. The author and his colleagues were soon convinced that x-ray treatment was too valuable a therapeutic agent to be denied to any pneumonia case Since then it has been used routinely.

The technic is given in Powell's own words, as follows:

"The technic I originally used gave good results and it has remained much the same as when we started We give 250 to 350 roentgens, using 135 kv. 3 mm. aluminum filter (on our equipment this gives radiation of 0.3 Å effective). We use a 40 cm. skin-target distance. The filter is heavier and the distance is greater than usually used in treating acute infections, but it tends to more homogeneously irradiate a large mass of solid tissue such as is present in a pneumonic lung. Also, the total dosage on the skin is larger than is generally used in acute conditions, but the depth dose is not large, and we think that our results warrant continuation of our present technic As soon as the diagnosis is made from history, physical and roentgen examination, and the blood count (this usually takes about 15 minutes), treatment is given anteriorly or posteriorly over an area a little larger than the involved portion of the lung A definite leukopenia, such as is found in some postinfluenzal pneumonias, is the only contraindication to roentgen treatment we have observed. We do not wait for sputum typing, but give a roentgen treatment immediately. Sputums are typed though as soon afterward as they can be obtained

"If the temperature has not returned to normal, or below, within 36 hours following the first roentgen treatment, a second treatment of 200 r is given over the opposite skin area roentgen treatment is given before consolidation is complete it may spread, but the patient shows the usual clinical improvement, and temperature, pulse, respiration and leukocyte count return to normal This is similar to the often made observation that the patient recovers clinically days, or even a week or 2, before the pulmonary consolidation resolves. A few cases with mixed infection

have required a third or fourth treatment, using, of course, successively smaller doses so as to avoid skin reaction. Mixed infection cases are more apt to recover by lysis after an initial drop from the high temperature to a moderate elevation above the normal."

The author's patients were treated in all stages of the disease, from the first to the eleventh day. Most of the patients showed relief of distress and general symptomatic improvement within a few hours. More than one-third of the patients showed a drop in temperature to normal within 36 hours from the beginning of the x-ray therapy. In a number of cases the temperature returned to normal in less than 12 hours.

The following case history, roentgenograms and temperature charts are shown to illustrate the results the author expects following roentgen treatment

Case I, white, male, aged 42, admitted on the third day of his illness, which started with a chill, pain in the left upper chest, high fever, and blood-tinged sputum. On admission to the hospital the patient had a temperature of 101 2° F (38 4° C), pulse 112, respiration 30 Leukocyte count 24,600, with 94 per cent polymorphonuclears, nuclear index 35 showed general mixed infection, few pneumococci not Types I, II or III Roentgen examination of the chest (Fig. 22A) showed consolidation of the left upper lobe and beginning consolidation in the right middle lobe On the morning after his admission, roentgen treatment was given and the following day his temperature dropped to normal. During the next 2 days it rose to a little more than 100° F. (378° C) after which it remained approximately normal. A roentgenogram 6 days later (Fig 22B) showed more than 50 per cent resolution. Figure 22C shows the patient's temperature curve.

Lest it be assumed that roentgen therapy makes the treatment of these cases too easy, Powell stresses the fact that pneumonia patients are sick patients, and must be treated as such. They must be watched carefully and given symptomatic

treatment when indicated. *Digitalis* is used by the author only when there is definite cardiac decompensation *Oxygen* is used when there is cyanosis or

ice caps and cold colon-flushes. The author does not like to use antipyretic drugs.

In summary the author states:

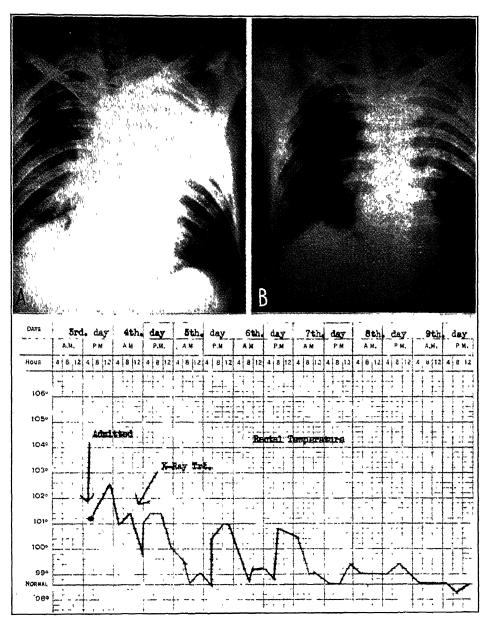


Fig 22-Case I (Powell Am J Roentgenol)

when the respiratory rate is so high that it is exhausting to the patient *Metrazol* is used as a respiratory and peripheral circulatory stimulant *Morphine* or *dilaudid* is given for pain when indicated Very high fever is usually controlled by

"In addition to the usual therapeutic routine, 105 cases of lobar pneumonia have been given roentgen treatment. Of these only 5 died. Thirty cases of bronchopneumonia have been given roentgen treatment and of these 4 died. Even if

the mortality had not been reduced so very sharply, the use of roentgen therapy in these cases would be justified by the relief or anxiety and discomfort experienced by the patients All Type II and Type III pneumonias treated with roentgen rays have recovered."

W. R. Scott¹⁴ offers a summary of 138 cases of pneumonia which passed through the x-ray department of the Niagara Falls Memorial Hospital during 1 year, October 1, 1937, to September 30, 1938 No case was refused x-ray therapy when it was requested by the attending physician, even though it was considered useless Whenever possible, the treatment was given as soon as the patient entered the hospital No areas of the chest were protected in pneumonia patients, the central ray being directed to the area of consolidation; in bronchopneumonia the therapy was centered over the area that showed the most confluence of mottling.

Of the 138 patients, 63 received chiefly x-ray therapy and of these 10 or 158 per cent died, 50 received no x-ray therapy but had radiographs of the chest taken and of these 10 or 20 per cent died. Thirty-four patients were neither radiographed nor given therapy, and the death rate for these was 441 per cent

The figures are further broken down into specific type of pneumonia present and age of the patient. The number of hospital days is recorded for patients receiving x-ray therapy alone, x-rays plus other therapy and no x-rays. They were on an average 10, 12 and 25 for bronchopneumonia and 12, 14 and 23 for lobar pneumonia.

Squamous Cell Carcinoma of the Extremities

H Charache¹⁵ points out that squamous cell carcinoma of the extremities is comparatively rare, comprising about 1

per cent of all carcinoma in different parts of the body It is 4 times as common in males as females, and the average age incidence is 63 years.

Volkmann's classification is generally accepted: (1) Those that develop on chronic inflammatory tissue such as ulcers, scars, fistulas, etc., (2) those that develop on warts, moles, congenital or acquired, (3) those that develop on previously normal skin

He states that the treatment is mainly surgical, for when a biopsy is taken the entire lesion can usually be removed. The superficial ulcerative type should be treated by radiation since there is usually concurrent infection. The prognosis is favorable in all cases as the clinical course is benign and metastases rare

Tumors of Bone

Radiation Therapy—J. S. Fulton¹⁶ takes up x-ray therapy of simple bone cysts, chondroma, angioma, benign giant-cell tumor, primary osteogenic sarcoma, metastasis, myeloma and Ewing's tumor. The general aim in treatment should be to deliver the maximum dose possible without exciting a severe reaction, and one should remember that bone, because of its calcium content and blood supply, reacts differently to irradiation than soft tissue

The author commonly gives from 2500 to 3000 r throughout the tumor zone in 3 weeks' time

Irradiation may arrest a simple bone cyst and induce calcification. It is the treatment of choice in benign giant-cell tumors and angioma. Chondroma may be expected to respond favorably if the tumor is of limited extent, or is so located that effective doses may be delivered.

Osteogenic sarcoma ordinarily responds poorly but when surgery is contraindicated, irradiation may be tried. In

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some cases it causes growth restraint. Metastases offer a favorable field for palliation and good results may sometimes be obtained by a single massive dose of from 1000 to 1500 r Irradiation relieves pain and uniformly produces a response in myelomas, thereby prolonging the life of the patient. It also benefits cases of Ewing's tumor and is possibly superior to surgery if the diagnosis is made at an early stage of the disease.

Cancer of the Tongue

S. Cade¹⁷ points out that 3500 people in England and Wales are victims of cancer of the tongue and mouth When comparing cancer of the tongue with cancer of other common sites, such as the stomach and the breast, the disease is more accessible and less virulent; furthermore, it is in one of the anatomical sites where the greatest progress has been made in the radiotherapy of malignant diseases

In most cases, cancer of the tongue arises on a precancerous lession such as chronic superficial glossitis, leukoplakia and gross dental sepsis. In addition to these, there must be some other factor such as an "inherent predisposition" of the tissues to undergo malignant degeneration. While we cannot control this, the precancerous state can be treated prophylactically.

In the tongue as elsewhere the gravity of malignant disease is due to its tendency to spread. However, here, early spread is solely by the lymphatics for a considerable time, and this is a favorable factor.

The natural history of cancer of the tongue shows 4 stages (1) Precancerous lesion, (2) cancer localized to the tongue, (3) local spread to the adjoining tissues; (4) lymphatic spread to the cervical lymph glands. The earlier the treatment is instituted, the simpler and

safer is the therapeutic measure. In spite of this, 75 per cent of patients die in the first 5 years following treatment.

The greatest hope of early diagnosis is the induction of "cancer consciousness" in the general practitioner. Every wart, ulcer, or nodule should arouse a suspicion and a biopsy taken to establish the diagnosis without delay. There are 2 conditions which require special mention: (1) Syphilis of the tongue, which is rare, but cancer of the tongue may occur in the presence of a positive Wassermann; (2) lesions of the posterior part of the tongue which are difficult to diagnose and spread rapidly.

Radium, x-rays and fulguration are the methods of choice today for this lesion Radiation may be (1) interstitial (2) teleradium or treatment by the radium "bomb" and (3) "contact" low voltage x-rays.

Interstitial radiation or needling is suitable for lesions of moderate extent situated anterior to the "V" of the circumvallate papilla. It has the following advantages; the period of irradiation is short, never over 1 week. A high tissue dose can be given with a small quantity of radium. Great accuracy of treatment can be achieved, and there is little radium reaction in the rest of the mucous membrane

Teleradium is the method of choice in the posterior part of the tongue. Needling in this location is technically difficult Five hundred times as much radium is necessary, and the rays are here directed through selected skin ports

Low-voltage "contact" x-radiation has only been in use for the past 5 years. The adequate penetration of the rays is limited to 1 cm, so this method is only applicable to superficial lesions. The advantages are simplicity, accuracy, less time, and hospitalization is not necessary. Fulguration is indicated in cases in

which the lesion is situated in a bed of scar tissue or when infection or edema render irradiation unsafe. It is also indicated in recurrences when further irradiation may lead to necrosis.

The ideal treatment of cervical nodes is wide surgical excision but this depends on the reaction of the primary lesion to irradiation, the condition of the glands, and the age and health of the patient When any of the above conditions render a block dissection undesirable, irradiation is indicated

Inoperable Carcinoma of the Larynx¹⁸

X-ray Treatment—Clinically and histologically there are 2 main varieties of larvngeal cancer That composed of undifferentiated cells having a great tendency to early and widespread dissemination in the loose connective tissue; and cancer composed of differentiated cells having a special affinity for the muscles The latter causes an immobilization of muscle without any tendency to dissemination Those composed of differentiated cells are in the domain of surgery, and usually are not curable by radiation because of the intimate relationship between carcinoma cells and muscle cells. They develop slowly and are generally of limited extent and of small size Regional adenopathy is rare The cells appear in a region in which a chronic inflammatory state has led to a special modification in the dense connective tissue

Cancers composed of undifferentiated cells are treated successfully and easily by x-rays. Because of their tendency to dissemination they are not biologically operable, even though they are technically operable Surgical intervention increases the danger of dissemination They are accompanied by early regional adenopathy whose involution is irregu-

lar, sometimes rapid, sometimes slow and sometimes regressive when they originate from the vestibule or the ventricular cavity.

Following are the methods of x-ray treatment. Cellulicidal technic, radioepithelite, and radio-epidermite.

The treatments that have been used until now have had for their aim the destruction of neoplastic cells, that is to say, a cellulicidal technic After some days of treatment, the cells are covered by a false membrane, when the cancer is composed of undifferentiated cells Depending upon the degree of differentiation, these false membranes appear between the fifth and thirteenth days after the beginning of treatment On the thirteenth day the false membrane appears on the normal mucosa (radio-epithelitis) In other words, when the cancer is composed of cells which are more radiosensitive than those of the normal epithelium of the mucosa the false neoplastic membrane appears earlier than the false membrane of the normal mucosa If the neoplastic cells do not show a false membrane until the sixteenth day, it shows that they are less radiosensitive than normal cells of the mucosa no cellular modification or diminution in size appears before the twenty-fifth day it is because of radiosensitivity of the cancer cells is about the same as that of the normal cells of the cutaneous epithelium. These normal cells are destroyed by radiation in 26 to 28 days (radio-epidermitis)

If the cancer cells are differentiated and have infiltrated the muscles they cannot be destroyed by irradiation. They are of the same radiosensitivity as the normal muscle cells and so irradiation would destroy the muscle cells just as easily as it would destroy the neoplastic cells The technic may be applied by daily or continuous treatment A total dose of 7000 r is delivered in 20 to 25 days for slightly differentiated cells; in 15 days for cancers composed of very differentiated cells; and 40 days for cancers which are completely undifferentiated.

Preparatory Treatment—If the cancer is very extensive and much infected, and the general state of the patient is bad, preparatory treatment lasting 13 to 26 days may reduce the infection and improve the connective and vascular tissues. The daily dose is kept as small as possible in order to avoid the development of fibrosclerotic connective tissue. This method was used for all cancers of the larynx in 1932 and seems to be the reason for improvement in 5-year results.

Periodic Treatment—The treatment is spaced so that the cellulicidal effect coincides with the moment of sensitivity of the normal mucosa. This treatment constitutes the only method which has given results for cancer of differentiated cells.

Palliative Treatment—The aim is to modify favorably the vasculoconnective tissue. The daily dose is kept as small as possible, 5 to 25 r.

The combination of surgery and x-rays in the treatment of inoperable or differentiated cancer of the larynx has not yielded better results than those obtained by surgery alone or x-rays alone

In the treatment of undifferentiated carcinomas which are apparently cured, there seems to exist a critical period appearing about 6 years after the irradiation. This critical period causes death 1, 2 or 3 years later, and if the patient escapes this critical period the cure appears to be permanent. An important factor, found to be of help in escaping the critical period, is to give a high

dosage during the last of the daily treatments, sometimes as much as 900 r being given.

Coutard analyzes his results carefully in regard to 5-year survivals as influenced by variations in the amount of radiation given. The preparatory treatment seems to have increased the number of 5-year survivals. His plan of future treatment is to begin with daily dosages of 5 r for the preparatory treatment and to build up to very high dosages, even as much as 900 r to be given the last day of treatment. In this way he hopes to avoid the "critical period" in the sixth year after the beginning of radiation therapy.

Metastatic Tumors in the Lung

Palliative Irradiation — A Brunschwig and A. Hamann¹⁹ demonstrate that immediate marked or apparently complete regression of pulmonary metastases in roentgenograms of the chest may not infrequently follow irradiation therapy Of 13 patients with pulmonary metastases from primary growths outside the thorax treated at the University of Chicago Clinics, 9 showed complete, immediate regression, 3 marked regression and 1 partial regression Five of the 9 died in 3 months to 1 year One died of intercurrent infection and 3 were alive at 19 and 21 months and 7 years

The doses varied widely and small to moderate ones were as effective as the larger doses

Carcinoma of Cervix Uteri

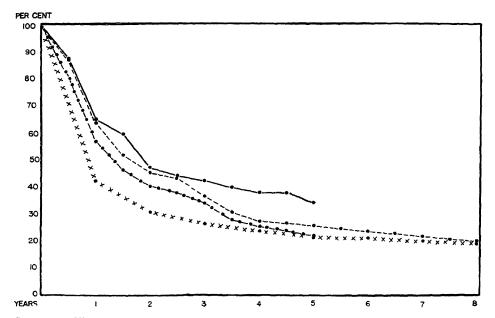
Management—H. F. Hare²⁰ outlines 3 factors upon which the management of carcinoma of the cervix depends (1) The host of the disease; (2) the extent of the disease in the host at the time the patient is admitted for diagnosis and treatment, and (3) the type of the lesion The first factor, although prob-

ably the most important, is an individual problem and thus far has not been successfully approached on a scientific basis. The second has been solved by the classification of the American Radium Society. The third is well established

The treatment of carcinoma of the cervix, with the exception of Grade I, strictly limited to the cervix, is a prob-

radon or radium is given locally in divided doses so that 6000 mg. hr. of radium with 2 mm. of lead filtration is delivered during the hospital stay

J. V. Meigs and H. L Jaffe²¹ trace 70 cases of carcinoma of the cervix treated at the Pondville Hospital for 5 years or more. The treatment consisted of x-rays through 4 pelvic portals, 8



lem for the radiologist Preliminary external irradiation is recommended before radium because (1) the peripheral growth in the adnexa receives the major portion of radiation effect from roentgen rays; (2) there is a low grade secondary infection which may be benefited, and (3) the primary tumor usually regresses and the physical condition of the host improves. A dose of 2000 r units is delivered to each of 4 skin portals, 2 anterior and 2 posterior at the rate of 100 r to each portal daily for 20 days.

by 10 or 10 by 10 cm. 2 anteriorly and 2 posteriorly. Each field received a total of 1500 to 2000 r (measured in air), the total dosage depending on the rapidity with which the treatment was given Daily exposures of 300 to 400 r were used, alternating the fields daily. Machine settings were 200 kv, 5 to 20 milliamperes, ½ Cu and 1 Al, 50 cm. S. T. D. At the end of that time 1500 millicurie hours of radium emanation (1 mm. Pt filtration) were given to the cervix. Four days later the radium treatment was repeated. The weakness

of this method lies in the fact that masses on the vaginal wall are not given sufficient treatment. This has lately been rectified by the use of interstitial radiation in the involved areas.

Their 5-year results are compared with Lacassagne at the Institut du Radium; Hurdon at the Marie Curie Hospital, London; Pitts and Waterman,

x-rays or a combination of both show the same life expectancy curve as predicted at this age. From this they conclude that cases showing no obvious disease at the end of 2 years have a good chance for recovery.

In Chart 2 cases with disease, involving the cervix or cervix and vagina are compared in regard to end results from

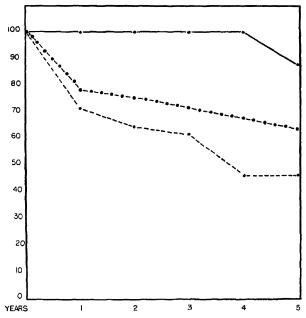


CHART 2—This chart graphically demonstrates that the fall of cases in comparable groups, A and B, is greater in the group operated upon than in the group treated with radiation. This chart is important to consider before deciding that surgery is better in early cases. A and B cases only ---- M G H surgical, 39 cases, ----- M G. H. radium, 28 cases; —--- Pondville, 8 cases (Meigs and Jaffe Surg, Gynec. & Obst)

Providence R I, Ward and Sackett at the Woman's Hospital, New York; and Healey and Frazell at the Memorial Hospital in New York Their results are better in nearly all cases than the latter 2 Pitts and Waterman did not include any cases with complete fixation of the pelvis or remote metastasis and therefore their relative cure of all cases appears better Lacassagne and Hurdon increase the number of their cures by better results in the more extensive lesions.

The authors point out (Chart 1) that after $3\frac{1}{2}$ years cases treated by radium,

surgery and from radiation Surgical cases do not do as well as the radiated ones

Weight loss seemed to be an important finding, since of 26 patients with a definite loss, only 6 are living and 20 are dead Biopsies were also taken before x-rays, at the conclusion of the first x-ray treatment and before the first radium treatment, at the time of the second radium treatment and before discharge The authors found that if radiation reaction is present and persists throughout the various biopsies, a fairly good prognosis can be hoped for. If no reaction

TABLE I

CARCINOMA OF CORPUS UTERI

RESULTS OF RADIATION THERAPY ALONE

Clinical Group	No of Cases	5-Year Survival	Free of Disease 5 Years or More	Death Due to Cancer			Death from
				Less than 1 Year	1 to 2 Years	2 to 4 Years	Other Causes in Less than 5 Years
Clinical Group I, uterus not enlarged .	24	58%	46%	17%	17%	0	8%
Clinical Group II, uterus not larger than 2½ months gestation .	40	55%	47%	0	15%	25%	5%
Clinical Group IIA, uterus larger than 2½ months gestation	7	0	0	29%	43%	28%	0
Clinical Group III, extension of cancer beyond uterus.	25	4%	4%	72%	16%	8%	0
All cases .	96	39%	32%	25°/c	18%	14%	4%

(Healy and Brown Am J Roentgenol)

is present or if there is actively growing cancer without reaction anywhere on the slides, the outlook is poor Uremia due to blocked ureters is one of the chief causes of death. This may be due to carcinoma or fibrosis from the radiation. Therefore urological investigations should be undertaken before, during and after treatment Any indication of ureteral block should be treated early

Carcinoma of Corpus Uteri

Radiation Therapy—W. P Healy and R. L Brown²² review 96 cases treated by radiation alone at the Memorial Hospital in New York All cases were proved histologically to be carcinoma. The cases were classified clinically and histologically and the end results correlated.

Symptoms began after the menopause in 88 of the 96 patients. The chief complaint was recurrence of bleeding between the periods if the patient was still menstruating. Pain in the lower abdomen and pelvis was present in 32 per cent

of the cases and was a significant symptom, since 87 per cent of these patients died of carcinoma In 50 per cent the duration of symptoms was 1 to 5 years.

The cases were placed in 3 clinical groups, according to the gross size of the uterus and palpable extent of disease at first examination Group I included those cases in which there was no palpable enlargement of the uterus and no extension beyond it, 24 cases fell in this group and of these 46 per cent remained free of disease for 5 or more years. Group II comprised those cases in which the uterus was slightly, moderately or markedly enlarged without evidence of extension elsewhere. These cases were further divided according to the size of the uterus, and it was found that of the 40 patients with a uterus not larger than a 2½ months' gestation 47 per cent survived 5 years or more, whereas the 7 patients with a uterus larger than this did not survive 5 years. This was believed to be due to the technical difficulty of deliver-

TABLE II

CARCINOMA OF CORPUS UTERI
RELATION OF HISTOLOGIC TYPE TO END-RESULTS

Histologic Type	No. of Cases	5-Year Survival	Free of Disease 5 Years or More (5-Year Cure)	Death Due to Cancer			Death from
				Less than 1 Year	1 to 2 Years	2 to 4 Years	Other Causes in Less than 5 Years
Adenoma malignum Grades 1 and 2 .	46	39%	30%	11%	24%	22%	4%
Adenocarcinoma, Adenocarcinoma Grade 2	29	41%	31%	31%	17%	10%	0
Adenocarcinoma Grades 3 and 4 Embryonal adenocarcinoma	18	28%	28%	45%	11%	5%	11%
Adeno-acanthoma	3	66%	66%	34%	0	0	0
All types .	96	39%	32%	14%	18%	25%	4%

(Healy and Brown Am J Roentgenol)

ing sufficient radiation throughout the greatly enlarged uteri. Group III comprised 25 cases with 1 5-year cure. Of these patients 72 per cent died in 1 year and only 12 per cent lived more than 2 years. For an analysis of these figures see Table I

Pathological data indicated that the histological type and grade of lesion do not strikingly influence the outcome from radiation therapy. These results are analyzed in Table II

The technic of treating these patients is given, and the authors state that cases of carcinoma of the corpus at the Memorial Hospital are now receiving 3600 mc-hr radon within the uterus, a pelvic cycle of 200 ky roentgen rays, 750 r to each of 4 to 6 portals at 70 cm, 0.5 mm. copper filtration, 30 ma Complete hysterectomy is done 6 to 10 weeks after irradiation is completed unless definitely contraindicated

Tumors of the Bladder

Roentgen Rays in Diagnosis and Treatment—G E Pfahler²³ points out

that since about 75 per cent of tumors of the bladder involve the ureters or urethral orifice, this method of treatment should be considered in a very large number of cases. The best results in diagnosis are obtained by the co-operation of the cystoscopist and radiologist Pneumocystography adds information that cannot be obtained by cystoscopy alone; for example, infiltration of the bladder wall The normal bladder will distend smoothly and evenly while an involved area will not distend and will produce an indentation in the general spherical outline

It is necessary to make roentgenograms in at least 4 positions. These will aid in providing a record of the size, extent and location and enable the therapist to better direct his treatment. In some instances bleeding may make cystoscopic observation difficult. Additional information of infiltration beyond the bladder wall can at times be obtained.

Films made in the prone position usually show the tumor best. About 86 per

cent of bladder tumors occupy the posterior or lateral walls and will be shown in contrast to the less dense air-filled bladder. Oblique films should also be taken. All fluid in the bladder should be removed, as soft tissue tumors when surrounded by fluid, cannot be demonstrated

The treatment of choice is that which will give the best results with the least risk or inconvenience to the patient. In the treatment of carcinoma of the bladder, excision or destruction will probably remain the first choice for those cases discovered in an early stage when the tumor can be completely excised or destroyed intravesically or when such treatment can be associated with the implantation of radium seeds into the base, without damage to the urethra or ureters. In only about 23 per cent can complete excision be applied without interfering with the ureters or urethra.

O'Crowley has analyzed the location of 854 tumors reported to the bladder tumor registry involving adjacent multiple areas and found that recurrence followed the initial surgical procedure in 462 per cent. Of 2597 proved cases of papillary carcinoma operated upon, 66 per cent were dead in 3 years. He further found that 766 per cent were located in the lateral walls, trigone and bladder neck, and involved the ureteral orifices.

In this group deep roentgen treatment will probably meet the above demands more completely than anything else that is known. The type of case that responds best to irradiation is the rapidly growing papillary carcinoma. The infiltrating type requires much more irradiation and when one has a patient nearly cured, there is a great temptation to carry on the treatment even though some risk is involved.

Radiation therapy consists of delivering enough radiation into the tumor tissue to destroy the cancer cells. This will require from 3000 to 4000 roentgens delivered into the tumor area. The treatment must be given in a manner consistent with the patient's general condition.

When a carcinoma of the bladder reaches a stationary stage and yet has not completely disappeared under irradiation, destruction of the remnants through the cystoscope may render the tumor more radiosensitive again. To obtain this result, however, it is necessary to give the radiation treatment rather promptly after the destruction

With the present technic, improvement may be expected in nearly all inoperable cases and probably a permanent recovery in 35 per cent.

Cancer of the Rectum

Radiological Treatment — E Berven²⁴ discusses briefly the histological structure of carcinoma of the rectum and points out the difficulties when the tumor and normal mucosa possess approximately the same degree of radiosensitivity. The results of treatment with irradiation show in general only isolated instances of permanent cure. The chief rôle of irradiation is palliation.

Cancer of the rectum is reported in 177 cases, of which 106 were inoperable and in these cases the treatment was found to have a considerable palliative effect. Radiation is also recommended for cases with large disintegrating operable tumors and all borderline cases since some of these may thereby become operable. It is stressed that preoperative irradiation of carcinomas of an undifferentiated type is highly important. Of the 106 inoperable cases given radiologic treatment only 13 per cent.

died during the first year, whereas the mortality is around 33 per cent without irradiation In early, highly differentiated, operable cases an immediate operation is indicated.

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THE SYMPATHETIC NERVOUS SYSTEM. SURGERY OF

By Paul G Flothow, MD.

ACHALASIA

Meade¹ reports the results of sympathectomy in the treatment of achaliasia of the cardia (cardiospasm). He opened the lesser omentum, severed the left gastric artery and nerves with it obtaining an excellent result. He reports only 1 case, and in this type of work a single case is of very little value from the standpoint of deduction. It would seem that the operation of severing the left gastric artery and nerves associated with it would perhaps leave the question of whether or not all of the necessary sympathetic components have been severed. Although it is a simpler operation than severing the splanchnic nerves, the latter is more complete and should give relief in physiologic cardiospasm.

ANGINA PECTORIS

Surgical Treatment—The REVIEWER has always felt that operations on the sympathetic nervous system in the treatment of angina pectoris are based upon sound anatomic bases, and that thyroidectomy for angina pectoris was without reasonable physiologic basis and therefore contraindicated

Ransohoff² relates his experience in the treatment of angina pectoris both by total ablation of the thyroid gland and by operations directed toward the sympathetic nervous system He treated 12 patients by total ablation and found that the procedure depressed the metabolism and reduced the cardiac work and the patient's activity The operation was followed immediately by remarkable im-

provement and decrease in precordial distress. The author now attributes this improvement to the severance of many sympathetic fibers during the course of the operation rather than to the removal of the thyroid gland The immediate good results, however, were not very lasting, and although there was only 1 postoperative death, only 1 patient was living in 1938, the operations having been performed from 2 to 5 years previously. The only surviving patient was one on whom the operation was not completed due to injury to the recurrent laryngeal nerve. The longest survival period was 3 years, the average being 6 months, and it was necessary to give thyroid extract constantly after the operations The author employs both surgical removal of the left cervico-thoracic chain and paravertebral alcohol injection. He has injected 10 cases with fairly satisfactory results, but feels that operation is much more satisfactory He reports 7 cases successfully treated surgically

Raney³ describes a new operation for the treatment of angina pectoris. His operation is based upon the theory that all of the efferent motor fibers to the blood vessels of the heart derive their origin from the second, third, fourth, and fifth thoracic rami to the sympathetic ganglia, or from ganglia cells below the fifth thoracic ganglion

He agrees with the concept that the pain of angina pectoris is due to spasm of the coronary vessels and aorta, and also feels that the vasomotor fibers cause constriction rather than dilatation of these vessels. He feels that the usual operative procedures succeed in interrupting the sensory afferent fibers, but leave certain motor efferent fibers intact, and that, therefore, although the tracts which carry painful sensation have been interrupted the patient may continue to

have the coronary vascular spasm although it is not associated with pain.

He, therefore, attempts to interrupt all of the motor fibers to the coronary vessels, leaving many of the sensory fibers intact, his feeling being that if no spasm of the coronary vessels can occur. there will be no anginal pain. Whether or not his concept is true, and whether or not it is based upon absolute anatomic and physiologic knowledge remains to be proved. His operation consists in removal of the third, fourth, and fifth ribs, exposure of the second, third, fourth and fifth thoracic ganglia and their rami, then section of all of the rami communicandi to the second, third, fourth, and fifth intercostal nerves, and section of the trunk between the fifth and sixth thoracic ganglia. The proximal end of the trunk is then sutured under the deep muscle layers to prevent regeneration He states that this operation has the added advantage of preventing occurrence of Horner's syndrome

BRONCHIAL ASTHMA

Leriche and Fontaine⁴ reported 14 cases of bronchial asthma treated by stellectomy in the period from 1926 to 1934 In 7 cases of unilateral stellectomy the asthmatic crises disappeared in 2 cases, but the operation failed in 5 At the present time, the satisfactory result of unilateral stellectomy in 1 case has lasted 13 years, and in the other case the attacks greatly attenuated reappeared after 7 years of complete relief from the attacks. In 4 cases of bilateral stellectomy there was immediate disappearance of the crises In 1 case, recovery was complete after $7\frac{1}{2}$ years. In the other 3 cases the crises reappeared greatly attenuated both in frequency and intensity The authors suggest that preliminary infiltration of the stellate ganglion before the operation is of value in attenuating or arresting the development of crises while the patients are being prepared for stellectomy.

Generally, but not in all cases, those patients who show a favorable reaction to injection of the stellate ganglion also show a favorable response to stellectomy

CAROTID SINUS SYNDROME

The literature contains a number of articles on the treatment of this rather spectacular, and to the patient most annoying, condition. Craig and Smith⁵ have classified this syndrome under "Hypersensitive Carotid Reflex," and divide the cases into 3 groups.

In the first group are those in whom the symptoms are mild and attacks are very infrequent. They state that no treatment is required in these cases other than reassurance

In the second group are those cases in which the symptoms are moderately severe and attacks more frequent. In these cases they recommend that the patient should be instructed to avoid turning the head quickly or forcefully, looking upward and stooping suddenly. Constriction of the neck should be avoided. If the spells are quite severe and occur at frequent intervals, sedatives, particularly phenobarbital, are recommended.

In their third group they place those cases that are severe, attacks of syncope are frequent, and in which medical measures have been without success. In this group they believe that surgical intervention is indicated. They report 13 cases treated surgically. Twelve of these were followed, with excellent results in 4, good result in 1, fairly good result in 4 and poor or failures in 3.

The operation consists of *perivascular sympathectomy* of the carotid bulb, removing the carotid body and carrying the resection well above and well below the carotid bifurcation.

The operative technic is well described by Leger.⁶ The operation must be carefully carried out so as to thoroughly denervate the carotid reflex mechanism and is fraught with little danger or technical difficulties.

CRANIAL POSTHERPETIC NEURALGIA

This is among the most distressing conditions with which the neurosurgeon has to deal. Why it did not occur to someone before this time that the pain of postherpetic neuralgia was perhaps mediated by sympathetic nerve fibers is difficult to understand. However, it remained for Hyndman⁷ to give us a new procedure for the relief of this distressing condition. He reports 3 cases in which he is certain that the pain of postherpetic neuralgia was caused by sympathetic nerve fibers

In his first case resection of the sensory root of the gasserian ganglion failed entirely to relieve the pain (This was the Reviewer's experience also in 1 case) However, he did succeed in relieving the pain somewhat by sectioning the supraorbital nerves and the blood vessels under the eyebrow, but the relief was far from complete

In his second case, having learned the lesson that section of the sensory root would not relieve the pain of herpetic neuralgia in the trifacial distribution, and feeling that the pain was due to sympathetic nerve fibers, he divided the left external carotid artery and resected the superior cervical ganglion. This failed to relieve the pain. He then sectioned

the ophthalmic and maxillary divisions distal to the ganglion, and the patient was relieved of pain.

In his third case, however, rather than do any of these operations, he felt that the proper procedure was sympathectomy. He performed a *left stellate ganglionectomy* plus the 3 thoracic sympathetic ganglia completely relieving the pain.

He concludes that the pain and hyperesthesia of postherpetic neuralgia are mediated by afferent sympathetic nerves, and that when neuralgia involves the head or neck, it may be eliminated by removal of the stellate and several upper thoracic ganglia on the ipsilateral side.

While his experience is a little limited to draw definite conclusion from, his experience plus the experience of many others in this field would certainly tend to verify his conclusions, and it is probable that at least in a large percentage of cases, sympathectomy will produce relief in cranial postherptic neuralgia

REVIEWER'S NOTE—The question can be definitely determined by diagnostic injection of the cervicodorsal sympathetic nerves

ESSENTIAL HYPERTENSION

The surgical treatment of this condition continues to be not only 1 of the most interesting but undoubtedly the most controversial subjects in the field of sympathetic surgery. Writers on this subject may be divided into 3 classes, those strongly in favor of the procedures, those just as strongly opposed, and a large group occupying the middle-of-the-road attitude with open minds, and feeling that the work should continue until a completely definite decision can be made.

My personal experience rather than increasing any skepticism that I may

have had, has made me more firmly than ever convinced that surgery is definitely indicated in properly selected cases of essential, and even in some cases of malignant hypertension As the years go on, and my earlier cases continue to carry on normal activities, I become more firmly convinced that these people are entitled to what the operation can offer them I am convinced that a number of patients whom I operated years ago would most certainly not be living now had they been denied operation. There is no question whatsoever that only a small percentage of cases obtains a marked and permanent lowering of the blood pressure, certainly not over 20 to 25 per cent That the vast majority of the rest of the cases without marked lowering of blood pressure levels is definitely and permanently improved clinically, is unquestionable

I wish to re-emphasize the fact that I feel we cannot evaluate the entire result of these operations entirely by measurement of blood pressure levels postoperatively I am certain of 2 things:
(1) That even though the mean blood pressure level postoperatively may be approximately that obtained preoperatively, (2) that the peaks where the pressure may surge 40 or 50 points above the mean levels are wiped out by the operation. This in itself is a tremendous advantage, and one which certainly warrants its performance even though nothing else could be offered the patient.

The other thing of which I a.n absolutely convinced, is that the operation produces beneficial results on the kidneys, the adrenals, and perhaps other organs of the body which we have no means of measuring.

Until some form of medical management can offer these patients anything at all comparable to that which surgery offers them, or until some operative procedure is evolved which produces better results than our present methods, I feel that it would be inhumane for this type of work to be allowed to fall into discard.

HYPERHYDROSIS

This again is not a particularly new subject, but will perhaps bear emphasizing and recalling to our minds since the subject has been more or less neglected in recent years. Occasionally one meets a patient in whom excessive perspiration of the face and hands becomes a major disability, and these people seek relief from this condition. Only a superficial knowledge of the sympathetic nervous system is required to understand the rationale of sympathectomy in this condition Removal of the proper sympathetic nerves assures absence of perspiration from hands and face recent report on the treatment of this condition by sympathectomy is by White 8

MIGRAINE

It seems a pity that the treatment of so disabling and so prevalent a condition should be so badly neglected. A great deal has been written during the past year on the medical management of migrame, and the use of various drugs in its treatment has been stressed. Of the various drugs which have been recommended, gynergen undoubtedly has been the most successful in the greatest number of cases none of these medical methods of treating migraine by drugs has done anything more than abort the attack after it has started, or to act as a prophylactic when an attack is about to occur. The only strictly medical measure which has afforded cure of the migraine attack has

been the discovery of allergic factors which may be the cause of the migraine attack.

Perhaps in the majority of cases prophylactic or therapeutic measures are sufficient, but there are vast numbers of people who suffer from severe attacks of migraine which are so frequent and so disabling as to render them practically incapacitated. In these cases no form of medical treatment seems to be of any avail other than to modify the attacks somewhat. Too often these people are told by their doctor, or are told by lay publications, and even in medical publications, that there is nothing that can be done for them, and that they will simply have to "grin and bear it" While this is undoubtedly true in some cases, a majority of them can be successfully treated by surgery of the sympathetic nervous system.

The procedure is simple. The first requisite is that the case must be 1 of true hemicrania, not the so-called migraine which is a term applied very loosely to many types of headache which are not true hemicrania. The diagnosis of true hemicrania is certainly not difficult, and need not be recounted here. A diagnostic injection should be done at the time the patient has an acute attack Needles are inserted at the cervicodorsal sympathetics, either by White's technic, that which I have described, or by a new technic described by Ochsner and DeBakev 9 The inferior cervical, the first and second thoracic ganglia on the side of the pain are injected with 1 per cent novocain. If they are successfully injected, a Horner's syndrome, namely, enophthalmos, develops, there is contraction of the pupil and absence of perspiration on the head, neck, shoulder, upper chest and arm on the side injected If the occurrence of a Horner's syndrome coincides with

complete relief of the migrainous attack, then one can be almost certain that surgical removal or destruction of the same sympathetic components will result in the cure of that individual.

I usually repeat the injections at a second attack as an added precaution against a surgical failure, because of the fact that at times these patients are so desirous of getting relief that there appears to be a psychogenic relief which may not be duplicated by operation. If there is complete Horner's syndrome, and the pain is only modified, not completely obliterated, one must be very wary of advising surgery unless a successive injection succeeds in completely relieving the pain. If the injection fails to relieve the pain, operation is obviously contraindicated.

My series is small, consisting of 5 cases. In all of these relief has been complete for several years. These were all cases of great severity in which the patients were at the point of suicide rather than living and suffering, and in every instance according to the patients themselves they have been "reborn."

One of these cases is particularly instructive Over 5 years have elapsed since a unilateral operation was done The operation was done on the side of the greatest intensity and greatest frequency of attacks, namely, the right side The attacks which she had on the left side were milder and rather infrequent Both sides were to be done, but the patient decided to put off the second operation, and left the hospital with a right-sided sympathectomy She has never had an attack of migraine on the right side, but continues to have the milder and less frequent attacks on the unoperated side.

Three out of 8 cases injected were not relieved by diagnostic injection and

were, therefore, not operated. Strangely enough, every case of true hemicrania that I have observed has been in a female

PAROXYSMAL TACHY-CARDIA

Leibovici¹⁰ and associates report the incident of a man 29 years old who developed a severe paroxysmal tachycardia following appendectomy. After all types of medication had had no effect on the tachychardia the authors resorted to the injection of 20 cc. of a ½ per cent solution of procaine in the left stellate ganglion with an immediate spectacular result. The pulse rate dropped from 180 to 70. Horner's syndrome appeared shortly after the injection and persisted for several hours The pulse rate continued to be normal, and there was no recurrence of the paroxysmal tachycardia

The authors pointed out that there is no longer any dispute regarding the fact that the sympathetic system plays a part in sinus tachycardia, and that surgical intervention on the sympathetic system has been employed with success in a number of cases of sinus tachycardia

SCLERODERMA

Surgical Treatment — This is not new As a matter of fact, it was 1 of the first conditions to be treated by sympathectomy since it was so often seen in association with Raymaud's disease. The Reviewer has had years of experience with scleroderma surgically treated by sympathectomy, and feels that unless the condition is a mild one, sympathectomy is not indicated in the treatment of scleroderma per se in advanced cases unless the operation is

directed primarily toward the relief of a coexisting Raynaud's disease.

Ochsner and DeBakey¹¹ again revive the subject of the treatment of scleroderma and state that the surgical treatment of this disease consists of *parathyroidectomy* and *sympathectomy*. They base the rationale of parathyroidectomy upon certain clinical and experimental observations which seem to indicate a definite physiologic disturbance in the calcium metabolism suggesting a hyperfunction of the parathyroid glands

The rationale of sympathectomy is based upon certain observations which indicate that the sympathetic apparatus is of pathogenic significance in certain forms of scleroderma. They note the fact that it is frequently associated with Raynaud's phenomena and other evidence of marked vasomotor disturbance They have performed parathyroidectomy and sympathectomy in 3 patients with scleroderma One and one-half years after operation there has been a slight improvement in 1, a moderate improvement in 1, and a marked improvement in the third case A fourth case in which sympathectomy alone was done reveals a marked improvement 17 months after operation. According to the author's own report, therefore, it would seem that the simpler procedure would be sympathectomy without the removal of the parathyroid glands. Here, again, we are faced with the problem of trying to draw conclusions from such a small number of cases

TABETIC CRISES

While the mechanism of tabetic crisis is not too definitely known, it seems apparent that the pain must reach conscious centers by way of the visceral afferent nerves from the abdomen. Most of the nerves, if not all of them, find

their way to spinal cord centers and consciousness by way of the celiac plexus and the splanchnic nerves. One way of treating tabetic crisis has been by interrupting these fibers by rhizotomy of the sixth to eleventh or twelfth thoracic nerves intradurally following an extensive laminectomy. This has been done with more or less indifferent results. A simpler way of accomplishing this denervation is by section of the splanchnic nerves bilaterally. In the past year I have done 2 such operations and in both cases the results have been highly satisfactory. The operation of splanchnic nerve section is not a dangerous one, and it seems to me that it is definitely warranted in severe cases of tabetic crises

In both instances in which the operation was done, it was on indigent patients at the charity hospital about whom the residents complained because of the fact that the attacks of crisis were so close together that these patients were almost permanent inhabitants of hospital beds. Over 6 months have elapsed since these operations were done, and neither of these patients has returned to the hospital for treatment of tabetic crises.

THROMBOANGIITIS

Adrenalectomy—In spite of the fact that it is almost universally conceded to be true that adrenalectomy is of no value in the treatment of vascular lesions of the extremities, Leriche¹² again reiterates the opinion that it is of definite value. He believes that it is the most efficacious of all methods of treatment when directed toward arteritis in certain cases.

He gives case histories of 3 patients, all of whom were relieved for long periods of time by unilateral adrenalectomy. He gives his results in the treat-

ment of approximately 1000 vascular lesions of the extremities by adrenalectomy, sympathectomy and arteriectomy.

THROMBOPHLEBITIS

Ochsner and DeBakey9 advocate the treatment of this distressing postoperative complication by sympathetic nerve block. They base their work on the results reported by Leriche, who believes that the clinical manifestations in thrombophlebitis are produced by the initiation of a vasomotor reflex as a result of impulses originating within thrombosed veins According to them, Leriche is of the opinion that there are 3 dominant factors in thrombophlebitis; namely, venospasm, the extent of coagulation and arterial spasm, of which venospasm is the most constant and significant. By blocking the sympathetic ganglia with novocain the vasomotor reflex is broken and the clinical manifestations relieved The authors agree heartily with Leriche in stating that the clinical manifestations in this condition are largely due to the vasomotor reflex which originates in the thrombosed vessel, and that the symptoms can be relieved completely, and convalescence materially shortened by blocking the sympathetics and breaking the vasomotor reflex However, it is their opinion that the clinical manifestations are due more to the arterial spasm than to venospasm They state that novocain infiltration of the regional ganglia has been successful in every instance of thrombophlebitis Immediately following the injection there has been complete relief of pain, which in some instances has been permanent. In other cases, subsequent injections have been required, but rarely has it been necessary to use more than 3 injections Within 24 hours the temperature recedes,

and is usually normal within 72 to 96 hours. The associated swelling of the extremity begins to diminish within the first 24 to 48 hours, and usually disappears completely within a week to 10 days. In over half the cases, the extremity has returned to normal size within 4 days.

VASCULAR LESIONS OF THE EXTREMITY

Sympathectomy — There is nothing particularly new in this field. It has always offered a fertile ground for controversy. Derom¹³ has carried out experimental work on dogs ascertaining the effect of various sympathetic operations on the reflex vasomotor changes of carotid sinus origin. On the basis of his experiments he has concluded that periarterial sympathectomy is of no value He decries mutilating operations on the peripheral nerves, such as alcohol injections, fascicular dissociation, and crushing between forceps, believing that they have little place in the treatment of any vascular disease since they are primarily destructive, and the beneficial results are at best short lived. (The RE-VIEWER concurs in these observations. his experience with this type of operation having been almost entirely bad, and in 1 case resulting in a fulminating gangrene which required amputation) He studied the various operations on the lumbar sympathetic chain, and does not agree with Danielopolu regarding the theory that simple section of the chain between the last lumbar and first sacral ganglia would affect the vasomotor response of the limb on the corresponding side. In order to obtain complete vasomotor loss in the lower extremity he found it necessary to remove the first, second, and third lumbar ganglia and the intervening chain He found that

unilateral adrenalectomy was without effect. He believes that the results of sympathectomy are frequently relative, and that it is not always necessary to obtain a maximum vasomotor change in order to produce complete vasomotor paralysis in order to save an extremity afflicted with Raynaud's or Buerger's disease. He is of the opinion that operations not entirely sound from a physiologic standpoint may at times be beneficial enough to warrant their use.

VESICAL ATONY

Huggins¹⁴ and his associates discuss the results of section of the principal nerves to the vesical sphincters in 18 cases of neurogenic atony of the bladder. commonly known as "cord bladder." The report marked improvement in 4 of 11 cases treated by presacral neurectomy, slight improvement in 4 others and no improvement in 3 They report 3 cases in children of urinary retention due to vesical atomy without other signs of somatic nerve disease or urmary obstruction, in which the retention was lessened by presacral neurectomy. They suggest that the condition in children may be analogous to Hirshprung's disease. They report good results in presacral neurectomy where bladder condition is due to localized lesions of the cauda equina or the sacral cord with the lumbar nerves being intact. Sympathectomy was not beneficial where the disease had produced injury to the pelvic nerve or sphineter with true incontinence as in tabes dorsalis

REVIEWER'S NOTE—In considering the question of sympathectomy for cord bladder, the physiology must be taken into consideration. It must be remembered that the sympathetic fibers are those which give the internal sphincter tone,

and inhibit the detrussor mechanism. If the detrussor mechanism has been damaged, then we have a marked imbalance with a preponderance of sympathetic influence, and in these cases sympathectomy is indicated. However, where both sympathetic and parasympathetic nerves are destroyed, sympathectomy can, of course, be of no value as it would simply mean removing an already functionless nerve tissue

VESICAL SPASM AND PAIN

There has been quite a bit in recent literature regarding the treatment of intractable vesical pain resulting from bladder infection by way of the visceral nervous system Nesbit and McLellan¹⁵ conclude that sympathectomy relieves the bladder pain not by removing the essential afferent pathways from that viscus, but by relieving spasm of the internal sphincter, and perhaps other parts of the bladder musculature. They state that the 1 constant predominating feature of all these cases is the presence of vesical spasm prior to operation, and that the constant postoperative result was relief from intolerable spasm, and the resulting ease of urination They state that it appears evident that section of the hypogastric nerves alone without division of the lateral sacral sympathetics provides adequate relaxation of the sphincter to relieve bladder spasm. They make the following statements.

- 1 The parasympathetic (sacral) pathways carry the essential afferent components of the bladder
- 2 The sympathetic (presacral or hypogastric nerves) pathways may or may not carry afferent pain components of the bladder
- 3 Division of the presacral nerves provide relief of vesical spasm and pain resulting from intractible bladder infection
- 4 Division of the lateral sacral sympathetics in addition to the presacral nerves accomplishes

this same end, but does not appear to be necessarv or desirable

- 5 Sympathectomy brings about the relief of spasmodic pain by relaxation of the vesical outlet and the detrussor mechanism It does not render the bladder insensitive to pain of
- Sympathectomy for the relief of bladder pain should be resorted to only in those patients in whom that pain is clearly demonstrated to result from spasm of the vesical outlet
- 7. Sympathectomy was not shown to cure the lesions of Hunner ulcer in cases reported

Schroeder and Cumming¹⁶ are not in agreement with the foregoing statement that excision of the superior hypogastric plexus alone is sufficient to relieve intractable bladder pain due to vesical spasm They feel that removal of the lateral sacral sympathetic chain should be added to the operation They advocate, also, the use of subarachnoid alcohol injection for the relief of certain types of vesical pain Hepler, in a discussion of this paper, makes the significant observation that one can determine whether or not the bladder pain may be relieved by sympathectomy by first injecting the presacral nerves, using the technic described by the reviewer. He suggests that if a diagnostic injection is made while the pain is being experienced, and this pain is promptly relieved, then presacral neurectomy may be done with the assurance that it will give relief of pain. If this injection does not relieve the pain, then a low spinal anesthetic may be given at the same level as the

proposed intraspinal injection of alcohol This would anesthetize the parasympathetic fibers in the third, fourth sacral roots, and also the somatic fibers of the third and fourth sacral roots. If this alone relieves the pain, laparotomy would be unnecessary, and simple subarachnoid injection of alcohol should suffice If pain is not relieved by either of the injections alone, but is relieved when they are combined, one then has some assurance that the combined operation will be successful. If the combined injections do not relieve the pain, suspicion is aroused that the symptoms are psychogenic

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THE TEETH

By Conrad F. Hellwege, DDS

Vincent's Infection

The Council of Dental Therapeutics of the American Dental Association presents a study of Vincent's infection 1

Vincent's infection is described in the literature under numerous terms, among them being: Trench mouth; ulcerative stomatitis, Plant's angina, Plant's ulcer,

Plant-Vincent infection, acute oral spirochetosis, acute ulcerative gingivitis, cancrum oris, ulceromembranous stomatitis and ulceromembranous gingivitis

It is an infectious disease of the oral mucosa, generally acute, but may be chronic Fetor, ulceration, swelling, tenderness of the soft tissues, gomphiasis, cervical adenitis and salivation are characteristic of the disease. Diagnosis is complicated by the fact that neither oral bacteria nor oral symptoms are absolutely specific If, however, a microscopic examination of a smear made from turgid, hemorrhagic, grayish slough-covered gingiva reveals a predominance of fusiform bacilli and spirochetes a diagnosis of Vincent's infection can be made. It may be necessary to perform serologic tests to differentiate from syphilitic infections, since the Borrelia vincenti and Treponema pallidum are similar morphologically Vincent's organisms are saprophitic anaerobes, which frequently enter as secondary invaders of previously debilitated tissue. In many cases of Vincent's infection, recovery occurs apparently without treatment. These findings cast doubt on the relationship of Vincent's organisms to the disease

The usual local signs of the disease are fetor, necrotic gingivitis, ulceration, oral sepsis and mucous patches Gomphiasis, mucosal eruption, glandular swelling, sore throat, dysphagia, salivation and capillary hemorrhage are less important diagnostically General symptoms are fever, malaise, constipation, restlessness, headache and loss of appetite Marked redness of the gingival crest and oral sepsis are among the first symptoms, followed shortly by gingival swelling and pain Ulceration, fetor and adenitis follow closely. Gomphiasis, dysphagia, salivation and hemorrhage develop concurrently as the disease progresses

Age incidence is insignificant; however, the young adult is more susceptible. The incubation period is unknown, since subclinical infection may be present before definite symptoms make their appearance. However, if the disease is acute, the patient reacts in 2 or 3 days The disease may become chronic in 7 to 10 days, resulting in borderline cases, difficult to recognize and cure. Since the oral symptoms of Vincent's infection are similar to those found in syphilis, actinomycosis, smallpox, varicella, acute tonsilitis, malignant leukopenia, leukemia, pellagra and beri-beri, a blood count is advisable; especially if arsenic therapy is contemplated.

With the full co-operation of the patient, prognosis is generally favorable. Patients of lowered resistance due to unhygienic living conditions, malnutrition or long-continued fevers may develop noma, with fatal results. Pleuropulmonary gangrene and infections of the accessory nasal sinuses are other reported complications.

Drugs used for topical application, supplemented by careful scaling and polishing of the teeth are classified as:

1 Spirocheticides

Neoarsphenamine—25 to 10 per cent solution in glycerine—applied to the dried mucosa 2 to 3 times daily and left for 5 to 10 minutes before being washed off

2 Caustics (not advised)
Phenol, 95 per cent topically

Silver nitrate, 35 per cent topically Chromic acid, 10 per cent topically. Trichloracetic acid, concentrated, top-

Copper sulfate, 10 per cent topically Zinc chloride, 10 per cent topically

3 OXIDIZING AGENTS

Hydrogen peroxide, full strength or diluted as a mouthwash.

Aromatic chlorazene, ½ teaspoonful in half glass of hot water as a mouthwash.

Potassium permanganate, 1:1000 or 1:5000 as a mouthwash.

4 BACTERIOSTATICS:

Viogen (1 Gm crystal violet plus 1 Gm brilliant green in 100 cc. of 50 per cent alcohol, topically).

Metaphen, 1:1000 as a mouthwash. Merthiolate, 1:1000, 1:5000 topically.

Extraction of irritating teeth is permitted only after the acute symptoms have subsided Cautery delays healing by spreading the infection

A thick paste of **sodium perborate** and water may be applied to the ulcerated areas and allowed to remain for 5 minutes after which it is washed off with warm water

Dentifrices containing sodium laurate, palmitate, myristate or oleate are indicated for prophylaxis rather than for curative treatment. In obstinate chronic cases potassium arsenite, US. P, or acetarsone may be prescribed

Smoking should not be permitted Diets rich in vitamins are essential

Bacteriologic Study of Careous Cavities

Basil G. Bibby, BDS PhD and Maynard K Hine,² MS., DDS, present the result of a microscopic study of cavity flora, including the diversity of organisms present and an approximate estimate of their numerical distribution. Smears were made according to Gram. The material was obtained from the teeth of children and freshly extracted adult teeth after the superficial débris was discarded.

The survey shows the wide ranges of variation in the flora of cavities and that there is no relation between type of cavity and bacterial flora. The gramnegative cocci consistently were more numerous than the gram-positive. The percentage of gram-positive bacilli including lactobacilli was low

A study of smears from a single cavity indicated that the percentages of organisms varied daily, however, they generally maintained their relative order in their occurrence. The percentage of gram-positive cocci ranged from 40 to 51; gram-negative from 20 to 29 per cent; gram-negative bacilli from 4 to 12 per cent, and gram-positive from 0 5 to 6 per cent Fusiforms ranged between 7 0 and 14 5 per cent Filaments ranged between 6.5 and 11.5 per cent

This study suggests that no specific bacterial species can be considered the cause of dental caries, since there is no significant difference between the flora of rapid and slow caries. The high percentage of gram-negative cocci suggests that these organisms are etiologic factors.

The low incidence of lactobacilli raised doubt concerning their importance in caries. There seems to be some constancy in the flora of the same cavity over short periods of time.

Dental Pain of Antral Origin

In order to promote a closer relationship between rhinologist and dentist J P Collins and E R Hargett³ call attention to the fact that tenderness and pain in the teeth and gums are not always the result of pathological conditions amenable to dental treatment Failure to recognize the fact that maxillary sinus disease may produce dental complaints may result in unnecessary extractions and construction of unwearable dentures

Patients during a submucous resection in removing part of the vomer or the base of the anterior septal cartilage frequently experience dental pains. This reminds the rhinologist that the nerve supply of the antrum and that of the maxillary teeth are derived from the same trunk, and that the apical nerve UROLOGY 1053

branches are in contact with the walls of the antrum for some distance. This association is called to the dentist's attention through study of roentgenograms and the knowledge of the danger of perforation into the sinus during extraction

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UROLOGY

By Elmer Hess, M D.

ANESTHESIA

C. R. O'Crowley and A. G Chmelnik, 1 E. B. Tuohy and G. J. Thompson² have reported many cases of difficult cystoscopy by the use of pentothal sodium intravenously, which is available in 0.5 Gm and 1 Gm. doses and is closely related to methyl butyl Only freshly prepared solutions of perfect clarity should be used. It does not disturb renal function Administration can be given ordinarily with a 20 cc syringe and the patient may be held for varying periods of time under the anesthesia. If the patient is a bad surgical risk and something more than an ordinary cystoscopy is being attempted, it may be given according to the technic O'Crowley Five per cent dextrose is given to combat the surgical shock and a 5 per cent concentration of pentothal sodium is given through the infusion tube. The tube is first clamped above, some 3½ inches from the vein, wiped with metaphen, and then pierced with the needle of the syringe containing the pentothal sodium solution. The first 3 cc. of pentothal sodium solution are given in 15 seconds, the administration is then halted for 35 seconds to permit the drug to exert its maximum effect. Another injection of 2 cc. is given in 15 seconds, the patient meanwhile counting 1 number per second during the whole process

of injection. A third administration of 2 cc., following a halt of 35 seconds as in the manner described, may be made until the desired anesthesia is obtained. This manner and rate of injection is adhered to both with the syringe technic and also when the more elaborate phleboclysis apparatus is used in conjunction with it. The intermittent and slow rate of injection is important and permits controllability of the drug's effect. It is seldom that over 6 cc. of the solution is needed.

A large group of urological procedures may be performed under this anesthesia, such as repair of hydrocele, suprapubic cystotomy, second stage prostatectomy, orchidectomy, circumcision, incision and drainage of perinephric abscess, varicocele excisions, bilateral epididymectomy, cystolithotomy, urethroplasty, ureteral transplantation to the groin, plastics on the perineum, multiple incision and drainage for extravasation of urine, retrograde dilatations for insertion of catheters, open epididymectomy, internal and external urethrotomy, fulguration of bladder for neoplasms and cystoscopy The age of the patient does not seem to interfere with its use; and it should be used in bad surgical risks.

E. B. Tuohy³ describes a new anesthetic agent, *metycaine*, for producing block anesthesia of the sacral nerves.

The anesthesia is much more rapidly produced and is much more enduring than when procaine is used. One 5 cc. ampoule of 20 per cent solution of metycaine is added to 95 cc. of physiologic solution of sodium chloride at a temperature of 99.6° F (37.5° C). The contents of another ampoule containing 1 cc of a 1:2600 solution of epinephrine is added to the solution of metycaine and sodium chloride. Under certain circumstances, such as marked hypertension or thyrotoxicosis, or in the presence of some cardiac condition such as angina pectoris, the epinephrine is omitted. Twenty-five to 30 cc. of 1 per cent metycaine are injected into the caudal canal and 15 cc of the same solution are injected transsacrally on each side, in the second, third and fourth foramina, 10. 3 and 2 cc, respectively, are used.

BLADDER

Painful States

The 1 constant and predominating feature of tuberculosis and incurable cancer of the bladder and interstitial cystitis is that vesical spasm is the cause of most of the trouble, while the constant postoperative result has been relief from this intolerable spasm R M. Nesbit and F. C McLellan4 conclude that division of the presacral nerves provides relief of vesical spasin and pain resulting from intractable bladder infections, that division of the lateral sacral sympathetics in addition to the presacral nerves accomplishes this same end but does not appear to be necessary or desirable, that sympathectomy brings about the relief of spasmodic pain by relaxation of the vesical outlet and the detrusor mechanism, that sympathectomy for the relief of bladder pain should be resorted

to in only those patients in whom that pain is clearly demonstrated to result from spasm of the vesical outlet, and that sympathectomy was not shown to cure the lesions of Hunner ulcer in the cases reported.

It has been the author's experience during the past few years to see a patient several years after sympathectomy was performed for interstitial cystitis. The patient was relieved of his urgency and pain for a period of 9 months after which the pain and irritability returned.

In discussing the relief of these painful conditions, J. P. Greenhill⁵ states that while sympathectomy yields gratifying results, it is also a serious abdominal operation and he has been able to control many of these painful bladder symptoms by *intraspinal injections of alcohol*. This is a simpler procedure and certainly warrants a trial as it is not attended by the risks of major abdominal surgery.

Technic of Intraspinal (Subarachnoid) Injection of Alcohol-No preliminary medication is given because we wish to observe the immediate effects of the injection Most patients with advanced carcinoma of the pelvic organs have much more pain on 1 side than on the other The patient is placed on the side opposite to that where most of the pain is present. A pillow or pad is placed under the pelvis and side to elevate the sacral and lumbar portions of the spine, the back is arched as much as possible, the body turned somewhat ventrally and the head lowered slightly By placing the patient in this attitude we raise the sacro-lumbar region of the spine to the highest level and at the same time make the posterior or sensory nerve roots lie horizontally. The anterior or motor nerve roots come to lie in a plane which is usually out of reach of the alcohol. Even if the motor nerves are

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not removed from the field of the alcohol as occurs in the cauda equina, they are not often affected because sensory nerves are more susceptible than motor fibers to the effects of alcohol.

Someone should hold the patient in the proper position. A weak solution of iodine or other antiseptic is applied over the lumbar and upper sacral regions. The injection is to be made in the second lumbar interspace. An ordinary lumbar puncture needle with a stylet is used. The needle is injected into the desired interspace just as for an ordinary lumbar puncture and novocain is injected into the skin before inserting the needle. After the needle is in the subarachnoid space, as evidenced by the flow of spinal fluid, 0.75 cc. of absolute or 95 per cent alcohol is injected into the cerebrospinal fluid. For this purpose it is best to use a tuberculin syringe so as to be sure not more than 0.75 cc. is injected Furthermore, the alcohol must be injected very slowly, drop by drop, taking about 2 minutes for the injection of the 0.75 cc The alcohol rises immediately to surround the posterior roots because the specific gravity of alcohol is about 0806, whereas that of the spinal fluid is 1.007-No attempt should be made to draw spinal fluid into the syringe to mix it with the alcohol because this is exactly what is not wanted. After the injection 15 made the needle is withdrawn and the puncture hole covered with sterile gauze and adhesive

Before the injection is completed, the patient will complain that the upper leg feels numb or hot and that the leg cannot be moved. The numbness is almost routinely experienced after the injection but disappears spontaneously after a few hours or few days in most of the cases. In spite of what the patient says concerning inability to move the leg, the latter can readily be moved when the

patient is requested to do so. At the same time the patient informs us of the numbness he also often tells us either voluntarily or in answer to our query that the pain has disappeared. The longer the patient is permitted to lie on the side, the better the results. Hence,

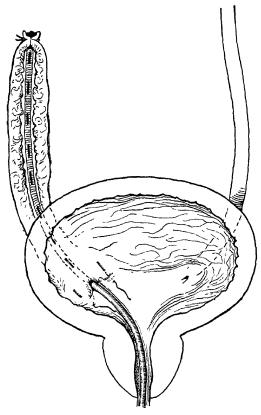


Fig 1—Recurrent carcinoma of ureteral stump after nephrectomy. Activated catheter is shown in position, in section, indicating the distribution of the Platinum Radon Seeds for even radiation of the entire stump. Removable Platinum Radon Seeds are shown implanted in the tumor involving the ureteral meatus and surrounding bladder wall (Radium Emanation Corporation)

the patient should be kept on the side for two hours after the injection. Then these individuals are permitted to get up and walk around. Some find difficulty in getting up from a chair because their "leg is asleep." Sometimes the leg feels heavy and the patient experiences some trouble in walking up steps because the knee flexes readily. These sensations

usually wear off in a few hours although in some patients they last a number of weeks. Nearly all of the patients who are ambulatory may be permitted to go home within 3 hours after the injection. No ill effects will be observed from this

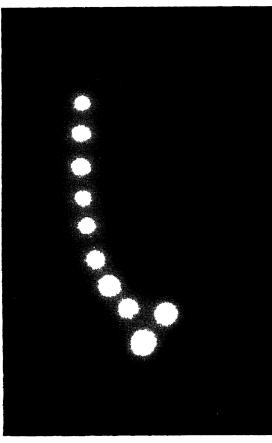


Fig 2—Phantom radiograph showing the effect of the radiation emitted by the activated catheter and implanted seeds shown in Fig 1 upon the photographic plate, illustrating the even distribution of the radiation sources along the length of the catheter (Radium Emanation Corporation)

procedure It is perhaps best, however, to keep a patient in a hospital for 24 hours after the injection. It should be emphasized that the intraspinal injection of alcohol may easily be carried out in a patient's home. This is important to remember because many individuals with cancer are bedridden at home and there is no need to subject them to the

inconveniences and expense of transportation to a physician's office or a hospital.

If the patient has pain on both sides an injection is made a week later with the patient lying on the opposite side. The same amount of alcohol is injected.

There are many cases of frequency and urgency of urination in women which are caused by cystocele, urethral stricture, acute inflammation in urethra or periurethral tissues. Dilatation of the urethra, correction of the cystocele and alleviation of the acute inflammation usually suffice to relieve these conditions for a long period of time if not permanently. There are conditions in women which require much more drastic procedures While this group of cases is not large, different men have reported successful results in the treatment of these cases by transurethral operations on the bladder neck, carried out in similar fashion to a prostatectomy in the male. Nesbit, Fite, Hicks, Van Houtum, Winsbury-White and Thompson have called attention to this particular type of bladder dysfunction G J Thompson,⁶ reporting a series of 24 cases, considers that the cause is apparently inflammatory with hyperplasia of the superficially lying epithelium at the vesical neck. In none of these cases was there present any submucosal glandular tissue. Folsom has described definite glands occurring in the vesical neck of the female and believes inflammation in such cases leads to symptoms Hyperplasia of such glands would explain dysfunction leading to urinary retention Each piece of tissue removed was sectioned; however, in none of them was glandular tissue discovered. Fibrosis also seems to be a cause. The cardinal symptoms are those of urinary obstruction Frequency, urgency with difficult urination and nocturia with varying amounts of residual urine are usually

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noted. In 6 cases, resection of the presacral nerve gave only temporary relief. Most of these cases at the present time are now being operated upon by the transurethral method, removing tissue from the entire circumference of the

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Fig 3—Double channel catheter, in partial section One channel is loaded with Platinum Radon Seeds evenly spaced, as shown in the illustration The free channel is a drainage channel for the prevention of hydronephrosis during treatment (Radium Emanation Corporation)

vesical neck, following operative treatment by dilatation until normal vesical function is re-established. In 24 cases, 35 transurethral operations were performed with the following results: Excellent in 14 cases, good in 5 cases, fair in 4 cases and a poor result in 1 case. Postoperatively, there is very often an irritating urinary retention. In all probability, this is due to postoperative intes-

tinal atony and the bladder retention is a part of the picture.

P. A. Marden and E. G. Williamson⁷ have been experimenting with **prostig**min and give it before and after operation to prevent this very annoying convalescent condition. The prophylactic dose is 1:4000; the therapeutic dose 1:2000. If the usual prophylactic routine seems insufficient to control urinary retention, the hourly administration of



Fig 4—Check test of activated catheter upon a photographic plate Catheter is placed in contact with plate and exposed for 15 seconds, giving the exact distribution of the seeds in the catheter. (Radium Emanation Corporation)

1 ampoule of 1:2000 prostigmin for 3 consecutive injections gives the desired results. They found no contraindications to the use of prostigmin and observed no untoward results

Tumors

In the diagnosis⁸ of tumors of the urinary tract it must be remembered that painless hematuria is the predominate symptom, and it is well established that if a patient is cystoscoped immediately after the first urinary hemorrhage, the

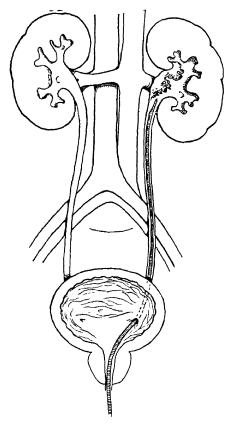


Fig 5 — Tumor of the kidney pelvis Long, activated double-channel catheter is shown in the ureter for the preoperative radiation of the entire ureter. The distribution of the Platinum Radon Seeds is shown in heavy outline (Radium Emanation Corporation)

vast majority of these bladder tumors may be discovered sufficiently early so that cure may be obtained. There are, of course, many diagnostic points that must be taken into consideration in the examination of bladder tumors. In a general way, it may be said that tumors with small pedicles are least malignant and that infiltrating tumors are almost always malignant. If one does not do a

complete urological study in cases of bladder tumors, it is obvious that many tumors of the upper urinary tract will be missed. There is a large percentage of bladder neoplasms that are reimplants from tumors of the upper urinary tract and so a simple cystoscopy is not sufficient. It is customary in most clinics to do intravenous urograms of the upper urinary tract, and if this does not prove sufficient then a suspicious lesion in either kidney must be verified by retrograde urography in spite of the added risk

There is an extremely high incidence of upper urinary tract pathology either as the result of the disease itself or as a complication of the disease or its treatment. These conditions must be recognized before intelligent treatment can be instituted C J E, Kickham and H L Jaffe⁹ cite Caulk who, in an analysis of 300 cases of vesical growths, found that damage in the upper urinary tract contributed to at least 50 per cent of the mortality rate. If treatment or the disease causes obstruction of either ureter. this information must be obtained at once so that appropriate measures may be taken to prevent renal insufficiency and death

Very often papillary carcinomas of the ureter will produce bladder tumors in and around the ureteral meatus. This condition frequently follows nephrectomy for papillary carcinoma of the pelvis of the kidney, and it has been necessary in a large number of cases to do complete nephro - uretero - partial cystectomy in these cases to prevent recurrence in the stump of the ureter or recurrence in the bladder. Again, there are many cases in which the general condition of the patient is such that such a drastic surgical procedure is attended with great risk Knowing that the vast majority of these cases presents recurrence in the ureteral

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stump and also in the bladder, E Hess⁸ has devised a ureteral catheter loaded with radium which may be applied directly in the stump of the ureter either as treatment or for the prophylactic destruction of the ureteral stump. This ureteral catheter has also been perfected so that preoperative irradiation may be

guration and the implantation of radium A few cases necessitate a suprapubic approach and a very few will require some short-circuiting of the urinary flow.

Much work has been done during the last year on intravesical roentgen therapy by means of the Chaoul roentgen apparatus. This shock-proof apparatus



Fig. 6-X-rays showing catheter in place, as shown by the Platinum Radon Seeds in the channel of the catheter (Radium Emanation Corporation)

given to the ureter This will not necessitate complete nephro - uretero - partial cystectomy in the favorable or unfavorable case but will permit the operator to do a simple nephrectomy, with excellent chances that recurrence will be prevented. The treatment of bladder tumors in the hands of the author has not changed materially in the last few years. All of these cases, for the most part, are treated through the cystoscope by ful-

gives low voltage roentgen therapy which can be given at the relatively short target-skin distances of 3 and 5 cm. or, if desired, by actual contact of the tumor with the anode or target that transmits the beam. G. T. Pack conceived the idea of applying this principle to the treatment of carcinomas of the bladder. The principle of marsupialization of the bladder over an extended time to permit fractionated doses of low voltage x-rays

to be applied through intravesical cones is new. Although this seems to be a distinct advance, the experience is limited and the curative value cannot be evaluated as yet. S. C. Levine, G. T. Pack and J. S. Gallo. ¹⁰ Suprapubic cystotomy is, of course, necessary.

onds, 1.2 milliamperes of current; filtration, 5 mm. of lead; half value layer of copper 11 mm.; focal skin distance 70 cm.

He considers wide surgical excision the most suitable treatment of bladder malignancy and when possible circumscribed growths are removed by opera-



Fig 7—Phantom radiograph showing the effect of the radiation emitted by the catheter, upon the photographic plate superimposed on the x-ray picture in Fig 6, showing the thorough radiation of the entire uretei (Radium Emanation Corporation)

F. H. Colby,¹¹ using a million-volt x-ray generator, has treated a small group of malignant bladder tumors and has studied the results of this therapy in a small series of cases. The present plan adopted for the treatment of bladder tumors is: A daily dose of 400 r units through 3 alternating portals, anterior pelvis, posterior left and posterior right; size of portals, 10 x 10 cm or 12 x 12 cm.; exposure time, 5 minutes 45 sec-

tion Super-voltage radiation is advised only when the extent of the tumor renders operation impractical or other factors make surgery unwise. For the most part debilitated individuals with extensive disease are radiated

It was found that the portions of the tumor which projected into the bladder cavity were affected considerably more than those which extended through the bladder wall. Other tumors are affected UROLOGY 1061

little, if any, and are considered radioresistant. The dosage so far employed is probably considerably less than could be used.

The future benefits of x-ray therapy as opposed to the present methods of treatment of bladder tumors are still problematical. If it is possible to diagnose the radioresistant from the radioactive tumors, certainly x-ray therapy is the preferable form of treatment in the latter cases. However, more experimental and clinical work is necessary before the value of the x-ray as the sole treatment of bladder neoplasms, can be accepted.

GENITOURINARY INFECTIONS

Mandelic Acid and Sulfanilamide -W. F. Braasch¹² in a general survey of the literature regarding mandelic acid and sulfanilamide is impressed with the fact that 2 entirely different principles of antisepsis are involved. Mandelic acid is the outgrowth of the use of acidification of the urine as a bactericidal agent. Some authors believe that the greatest antiseptic action of this drug lies in its ability to acidify the urine and that the specific antiseptic qualities of the drug itself are of less importance. When the pH of the urine is 55 or higher, the drug has very little effect, while the results are greatly enhanced if the pH of the urine is 50 Sulfanilamide, on the other hand, acts in an entirely different manner. Its action is not based on the acidity of the urine and no one knows exactly how it does exert its influence The effects of the drug in the urinary tract differ from that in the other tissues of the body The concentration of sulfanilamide in the tissues and in the body fluids is much less than in the urine If the concentration of the

drug were the same in the urine as it is in the tissues, this concentration would be inadequate for the elimination of bacteria in the urinary tract. The drug does not have direct antiseptic action in the body fluids but has a toxic effect on bacterial growth; while in the urmary tract, it is eliminated in sufficient concentration to make it bactericidal. This bactericidal value seems to be enhanced in the presence of an alkaline urine. Mandelic acid is used principally in the treatment of infections by the colon bacıllus; sulfanılamide, on the other hand, is used in infections caused by the colon bacillus, certain of the streptococcic group and a few of the staphylococcic group. Sulfanılamide is particularly valuable in treating those types of organisms which have urea-splitting properties, such as the proteus. One of the streptococcic groups which sulfanilamide has little or no effect upon is the Streptococcus fecalis and in this particular coccal infection, mandelic acid seems to have a specific action.

In the use of sulfanilamide there are certain untoward symptoms which, of necessity, must be carefully observed and which will contraindicate the further use of the drug or necessitate cutting the dosage below the point of toxicity. Nausea, headache, dizziness, fever, acidosis and leukopenia call for immediate discontinuance of the drug The cyanosis which is so common even in small dosage is not considered to be due to hemoglobinemia, and it seems to disappear upon discontinuance of the drug and has no great clinical significance. As a matter of fact, the author pays little or no attention to cyanosis but lays great stress upon nausea, headache and dizziness

S A. Vest, J H Hill and J A. C Colston¹³ note in some experimental work on infections with sulfanilamide that the drug has a directly bactericidal

action in urine infected with Staphylococcus aureus, Escherichia coli, Aerobacter and Proteus. They have noted that the drug is particularly effective according to the numbers of organisms in the urine, the Aerobacter being the most resistant of the organisms studied. They believe that sulfanilamide, even when used in moderate dosage and even though frequently discontinued because of disagreeable symptoms, is a much more powerful urinary antiseptic than mandelic acid.

S. McMahon,¹⁴ experimenting with mandelic acid, has used it intravenously on a large series of dogs. The investigation has not as yet been followed up in its clinical application to the human being. However, certain facts have been demonstrated and these should be noted. Intravenous injections of sodium mandelate did not affect the hydrogen ion concentration of the urine nor did they cause hematuria, albuminuria, or presence of casts in the urine. Massive doses caused impairment of kidney function, with quick recovery, moderate doses did not affect kidney function as shown by the nonprotein nitrogen estimations. Intravenous injections of $1\frac{2}{3}$ ounces (50) cc.) of concentrated solution, 20 per cent, show very high concentration of mandelic acid excreted for the first 2 hours Complete autopsy examination of some of the dogs showed changes in the tissues of kidney and liver, and he concludes that the drug caused definite changes in the tissues of the kidney and liver, but that these changes were easily reparable. It is believed, therefore, that a 20 per cent solution of sodium mandelate with the pH adjusted to 7.2 could safely be given intravenously, and that the high concentrations obtained in the urine might have a distinct therapeutic advantage It must not be forgotten that in coccus pyelonephritis, neoarsphenamine given intravenously is a very valuable and effective treatment. S. H. Johnson, ¹⁵ in discussing the various drugs used, concludes that although pyridine and sulfapyridine may possess superior efficacy, sulfanilamide is the most efficient chemotherapeutic agent in the treatment of gonorrhea, and that uleron (di-methyl di-sulfanilamide) and disulon (sulfanilyl-sulfanilamide) are at present too dangerous to use in the treatment of urinary tract infections.

Sulfapyridine—This brings up a discussion of sulfapyridine which is being frequently used not only in the treatment of urinary tract infections but also has widespread use in the treatment of pneumonia. It has been observed that after the use of this drug, calculi may form in the urinary tract and that these calculi are formed of acetylsulfapyridine. This probably would contraindicate the use of the drug in pneumonia in those cases where known obstructive urological lesions exist and is a complication that must be taken into consideration if this drug is to be exhibited in certain types of urinary infection. P. Gross, F. B Cooper and M Lewis¹⁶ have discovered that these uroliths of acetylsulfapyridine may disappear with overdilatation of the ureters and renal pelves following the discontinuance of the drug

Gonorrhea

F. G. Harrison¹⁷ emphasizes the fact that many of the patients who have responded to short courses of treatment by *sulfanilamide* are clinically relieved and have no subjective symptoms but that in many cases these patients become carriers and cannot be considered as cured.

There is no doubt that the drug is eliminated in the prostatic secretion as well as in the urine in bactericidal concentration, and that it has no effect on the motility or longevity of the sperm

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J. I. Farrell¹⁸ points out that patients with diminished kidney function do not tolerate the drug in the large doses used in the treatment of gonorrhea.

E. G. Ballenger, O. F. Elder and H. P. McDonald, 19 in a discussion of the treatment of gonorrhea, have combined the sulfanilamide treatment with the hyperpyrexia treatment and believe that 90 per cent of the cases of resistant recurrent infections can be completely cured and that the remaining 10 per cent will respond to both of the above methods of therapy plus local measures. Their plan consists of a series of 3 or 4 fever treatments given every other day combined with an adequate dosage of sulfanilamide The patient is given 60 or 80 grains (4 to 53 Gm) of sulfanilamide a day, for 2 days previous to the treatment, and then 80 grains (53 Gm) daily during the period of treatment. Too little sulfanilamide tends to offset the advantages which accrue from the combination of these 2 potent agencies All patients are closely observed and hospitalized for fever treatments. An insulated cabinet and short wave diathermy unit are used Warm air is kept circulating throughout the cabinet by means of an electric fan and an oral temperature of 103° to 104° F. (395° to 40° C) is sought This is usually maintained for 3 or 4 hours, varying with the general condition of the patient. All patients are watched and rechecked for a month or longer following the treatment and the usual tests are employed to determine whether or not the gonococci are completely eradicated Great attention is paid to the elimination of foci of infection

KIDNEY

Adenosarcoma

Adenosarcoma of the kidney or the Wilms tumor is probably the commonest

malignant neoplasm of childhood. H. D. Kerr²⁰ reports on 14 patients. The first symptom is a painless enlargement of the abdomen, frequently discovered accidentally and examination reveals that a large mass is present in the upper abdomen. Hematuria may be the first symptom. Metastasis occurs most frequently to the lungs, occasionally to bone. Patients who live 5 years or more after the beginning of treatment are rare and are worth reporting. Many patients have been improved under irradiation therapy alone and others have apparently been benefited under surgical treatment. Kerr believes that irradiation and operation should be combined. His irradiation technic is as follows: In general, we have used 200 kilovolts and 8 or 20 milliamperes, according to the available machine, Thoraeus filtration (effective wave length 0 135 angstrom unit and half value layer 195 mm of copper) or 0.5 mm of copper (effective wave length 0.16 angstrom unit half value layer and 095 mm. of copper) with a distance of 50 cm and anterior and posterior 10 by 15 cm. or 15 by 15 cm ports, depending on the size of the mass A dose of 200 roentgens a day to each part is given till a total dose of from 3000 to 4000 roentgens, as measured in air, has been When pressure of work has made the University's three 200-kilovolt machines unavailable, we have not hesitated to use 135 kilovolts with filtration by 025 mm of copper and have found that regressions of the primary tumor have occurred as soon as when the higher voltage was used. For the 2 living patients (5 and 9) second courses of treatment were given to the primary area. but this is also true of 6 of the others. It is felt that this is worth while. remembering that damage to the skin may result. Pulmonary metastases should be treated, as indicated by case 9, in

which 3 pulmonary nodules have disappeared after irradiation, and case 3, in which they disappeared but the patient succumbed to local recurrence and metastases to the bone. The former patient is still living, without evidence of neoplasm, 50 months after admission and 54 months since the onset of symptoms.

Operation should not be delayed longer than 6 or 8 weeks following irradiation One of his patients had irradiation followed by operation but died of generalized metastasis and recurrence 47 months after admission Another patient is living after 84 months, the parents refusing to have the affected kidney removed He feels that this is a fortunate rather than a logical result because no one can be certain that these tumors will contain different cellular elements and that while some of these tumors respond rapidly to irradiation, others respond not at all. For this reason, he feels that irradiation should be followed by nephrectomy

Calculous Disease

The effects of sulfapyridine in creating urmary calculi have already been discussed; however, the rôle of this drug in the treatment of children has not been sufficiently emphasized Out of 40 patients treated by sulfapyridine, 5 cases suffering from general nutritional deficiency, dehydration and polyavitaminosis, developed renal complications, the principal symptom of which was hematuria. One of these patients died of uremia as a result of bilateral complete urmary obstruction, proven at autopsy The hematuria is believed to have been caused by uroliths of acetylated sulfapyridine In the event that any child taking this drug for any condition should have symptoms of anuria or urinary obstruction, the drug should be immediately discontinued and every effort made to counteract the condition by cystoscopic

examination with ureteral manipulation or by an emergency nephrostomy.²¹

In many cases of calculous disease of the kidney, the symptoms are not typical. If the calculus is in the lower ure ter, the symptoms may be referred to the hypogastrium on the affected side. If above the brim of the pelvis, the symptoms may be epigastric or gastrointestinal and may be very confusing, while huge staghorn calculi of the renal pelvis may exist for years and give no symptoms of any kind unless some part of the large calculus breaks off and becomes engaged in the ureter Many cases have been operated upon for acute appendicitis where the symptom causing pathology was a stone in the lower right ure-Pelvic inflammatory disease may be simulated by low-lying stones in both lower ureters Wherever there are vague abdominal symptoms, the taking of a plain x-ray film will usually rule out a large percentage of these renal and ureteral stones and will aid materially in the diagnosis between intra-abdominal conditions and calculous disease in the urmary tract

B Davidson²² cites 2 cases of silent calculous disease. In the first case an intestinal obstruction was diagnosed 3 years previously to the discovery of the calculi, and in the second case, a female, age 47, was sent to him to discover the cause of a pyuria which had existed for 6 years. Plain x-rays of the urinary tract in both cases proved the presence of the disease.

Essential Hematuria

Most urologists believe that the diagnosis of essential hematuria should never be made, that if there is bleeding from the urinary tract there is a definite reason for it. However, there is a large number of cases where kidneys are at times sacrificed because of unilateral

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bleeding and the pathologist is unable to find anything but a perfectly normal organ. This is a dangerous diagnosis to make. C. E. Burkland²³ has pointed out that it is purely clinical and arrived at by exclusion. He believes that essential hematuria is a result of increased capillary permeability in the kidneys and that this increased permeability is due to a defect in the intercellular cement substance in the endothelium of the capillaries, permitting the blood cells to migrate through their walls with relative ease. In 1926, Wolbach and Howe showed that 1 of the main functions of vitamin C is to promote or regulate the formation of the intercellular cement substance In view of these observations, he used vitamin C in the treatment of 4 cases of so-called essential hematuria. The hematuria subsided after the patients were given intravenous injections of vitamin C in the form of the sodium salt of cevitamic acid in sterile water. A decrease in the hematuria was noted on the oral administration of vitamin C in the form of cevitamic acid tablets and fruit juices. No reactions were reported after large doses intravenously He concludes that in view of the efficacy of the treatment, cases of essential hematuria might be considered as subclinical forms of vitamm C deficiency, not giving the more definite expressions noted in the more severe forms, such as scurvy

Pyelonephritis

It is generally recognized that there are 2 distinct types of renal infection, according to W. F. Braasch²⁴; namely, a primary hematogenous infection, predominating in the renal cortex, and a lesion predominating in the central portion of the kidney which is usually called pyelonephritis. The path of infection with pyelonephritis is generally regarded as ascending rather than blood borne and

the bacteria usually belong to the bacillary group. To repeat, there are 2 distinct types of renal infection: type 1, the cortical, hematogenous infection, often requiring surgical treatment, and type 2, pyelonephritis, usually ascending from the lower levels of the urinary tract, with predominant bacillary infection, and seldom requiring surgical treatment

Acute pyelonephritis is by far the commonest lesion in the genitourinary tract occurring very often in the female. Most of these cases are of short duration and are self-limited. When the infection persists longer than 4 or 5 days and when it is accompanied by fever and chills, Nature is materially aided by the administration of any of the various chemotherapeutic agents now available.

The second form of pyelonephritis is characterized by recurrent attacks of acute pyelonephritis. The periods of infection persist for several weeks or months and recur after a variable lapse of time. In the interval, although the patient is free of symptoms, careful and persistent search of the urine will often show the presence of a few bacteria, indicating that the renal infection in most of these cases is dormant rather than eliminated

The third type of pyelonephritis is the chronic type and is the most difficult to overcome. Usually it involves both kidneys, runs a chronic course, and unless complications occur the only symptoms are dysuria and frequency of urmation. This disease is usually secondary to infection from the lower portion of the urmary tract. The causative organism must be determined to exhibit intelligently the proper chemotherapy. Surgical intervention in chronic pylonephritis is usually not indicated. If the pyelonephritis is associated with pyelectasis, renal lithiasis and other obstructive lesions, it

is necessary to relieve the underlying condition by surgical measures.

Respiration Pyelography

E. Hess²⁵ offers the following summary and conclusions on respiration pyelography:

Respiration pyelography is simple and easy to perform. It must be done under costoabdominal breathing.

It is of value in the study of normal kidneys where it is necessary to decide whether a low position of the kidney is permanent or temporary and to evaluate kinks in the ureter.

As a differential diagnostic sign between perinephric and subdiaphragmatic abscess.

As a checkup upon kidneys which have been operated upon for various reasons.

As an aid in the diagnosis of upper ureteral and renal calculi and in the differential diagnosis between gallstones and right renal calculous disease.

As an aid in planned operative procedures, in pyelonephritis, nephrosis, tuberculosis, and tumors of the kidney

TESTES

Traumatic Epididymo-orchitis

G E Slotkin, of Buffalo, New York, brought out the subject as a compensable disease in industrial accidents. This caused considerable difference of opinion in the minds of many competent physicians as to whether or not this disease is and should be compensable.

G. H Ewell,²⁶ in discussing a number of cases of the condition, says that these cases of epididymitis or epididymoorchitis provide evidence of inflammation and the alleged trauma is supposed to be a contributory factor. He raises the pertinent question as to whether trauma can intitiate epididymo-orchitis or light up

some dormant pathological condition and whether or not direct trauma or strain can precipitate a direct attack of the disease. Wesson, who has written extensively on the subject, states that an epididymitis is secondary to a urethritis or seminal vesiculitis and its occurrence depends on the virulence of the organism and the susceptibility of the patient. The extension to the epididymis evidently appears whether the patient is confined to bed or receives a blow on the testicle. Crane, in discussing epididymitis and its development, believes that the disease occurs spontaneously without being associated with trauma and believes that a minor injury is given credit for the sudden onset of an epididymitis when in reality the inflammatory process already existed and the trauma merely called at-Rolnick does not agree tention to it with these beliefs. There is no question that infections of the epididymis are secondary to infections of the seminal vesicles and that in a small percentage of cases hematogenous infections of the vesicle and posterior urethra take place Ewell's experiences lead him to believe that clinical attacks of inflammatory epididymo-orchitis can be and are precipitated by either direct or indirect trauma This may be accomplished by lighting up a dormant infection or by lowering the threshold of tissue resistance or by inviting infection from some distant focus That particular strain serves to force infected material, such as urine and prostatic fluid, along the lumen of the vas

In discussing this paper, Wesson decries the attempt to make epididymoorchitis of traumatic origin because of the medical legal importance of the subject and believes that unless we check the tendency to make trauma again the universal etiologic agent, we are shortly going to witness the beginning of the end of the private practice of medicine UROLOGY 1067

E. Cathcart believes that the difficulty does not lie with our opinion as to whether epididymo-orchitis is traumatic or not but that the social-economic aspect of the disease is an insurance problem and not a medical one. The treat ment is the same regardless of whether the origin is traumatic or infectious; rest in bed, elevation of the testes on a bridge, ice and urinary antiseptics, depending upon the nature of the causative organism, opening and draining if abscess takes place either in the epididymis or testes and, in some cases, castration is necessary.

Testosterone Propionate

A great deal of work during the past few years has been done in testicular deficiencies with testosterone propionate Much has been written for and against the use of testosterone propionate in certain clinical types of cases. However, it has been possible during the conduct of the research work in the laboratory and at the bedside to note certain facts P McCullagh²⁷ summarizes these In cases of severe prepuberal hypogonadism, injections of testosterone propionate in the doses indicated have been followed by symptomatic and anatomic changes in approximately the following order Penile erections occur promptly, and there is an increase in the pubic and axillary hair. The penis grows rather markedly, the scrotum less so, and the prostate growth appears to lag perceptibly in proportion Nocturnal emissions occur and the quantity of semen increases. No diminution in sperm count or inhibition of sperm production has been obvious where sperms are present, though this may not be so in cases in which there are a normal number of spermatozoa before therapy The larynx grows and the voice becomes lower Facial acne appears and the beard grows. Epiphysial closure has not exceeded its expected normal rate in cases in which testosterone propionate alone was used and in 1 case has not increased in 4 years in spite of marked advance in puberty. No constant change in basal metabolism has been observed. In cases of functional hypognadism in the adult this treatment has been followed by complete relief of nervous and sexual symptoms. In castrates, nervous and vasomotor symptoms and impotence can be abolished by sufficient doses.

That the effects of various drugs to stimulate growth of the external genitalia is not without danger has been brought out by Dr H. L. Kretschmer, who says that the indiscriminate use of these drugs might be attended by very undesirable consequences particularly in the treatment of undescended testes and as yet we do not know whether or not there is a deleterious effect on the spermatic function. The cases on which these substances are to be used must be very carefully selected and the dosage must be very carefully administered under thorough control and observation.

Undescended Testicle

W. O. Thompson and N J Heckel²⁸ have the following to say concerning this condition: Since Schapiro's report 8 years ago, testosterone propionate has been used extensively in the treatment of this condition. In spite of numerous observations in other clinics showing a high incidence of successful results, we have consistently been unable to produce descent in most instances of true cryptorchidism. In order to explain this discrepancy a critical survey of the problem is desirable.

In our series only 20 per cent of all the testes descended, and descent occurred in only 27 per cent of the patients under 16 years of age. The difference

between the high percentage of successful results reported by most other observers and our own percentage may be attributed in part to our exclusion, except in the beginning of the study, of all testes of the migratory or retracted types.

It is necessary in view of the observations made by these investigators to maintain an open mind on the treatment of undescended testes with the anterior pituitarylike principle. While the importance of bringing the testes into the scrotum at the earliest possible age has not been overestimated, perhaps the wisest course is to administer this material cautiously and carry out operative procedures if descent fails to occur Susceptibility to the anterior pituitarylike principle varies markedly, so that dogmatic statements about the size of the dose and the duration of the treatment cannot be made. As a rule, in successful cases, descent of the testes occurs within 2 months after the daily administration of from 100 to 1000 rat units is begun. It must be remembered that genital growth may be so markedly produced by this material that changes simulating premature puberty may result, and excessive genital growth should be avoided Again the question of what effect this would have on subsequent spermatogenesis, skeletal growth and social adjustment must be carefully ascertained If the descent of the testicle is associated with hypogenitalism, genital growth is to be desired and much larger doses are to be administered over much longer periods. One of the values of the administration of the anterior pituitarylike principles is the ability to decide at an early date between the testicles which require surgical intervention and those which do not

H. Wohl²⁹ calls attention to the fact that in the bilateral cases, patients over

14 years of age are not particularly benefited by endocrine therapy, while boys from 5 to 9 responded even with small doses. The important fact has been observed that endocrine therapy increases the size of the undescended testes and prepares them for later operation. In the unilateral cases he noted that there was no endocrine effect on the testicle already in the scrotum, that this therapy will not cause a unilateral undescended testicle to descend into the scrotum.

R. E. Cone³⁰ calls attention to the fact that most of these boys with undescended testicles will spontaneously have the testes descend at or near the age of puberty. This is due, of course, to the natural endocrine stimulation supplied the testicle at that time. If the testicle has not descended or been brought into the scrotum at or near the age of puberty, definite degenerative changes occur which result in sterility. Often these degenerative changes are the result of the inability of the testicle in its undescended position to respond to the hormonal stimulation incident to normal puberty This hypothesis is suggested by some recent experiments on rats Emphasis is placed upon the fact that there is still considerable controversy over the treatment of cryptorchidism Most of the men feel that some form of operative procedure is essential and that the hormonal treatment is only helpful Emphasis is also placed on the fact that the weight of evidence supports the conclusion that the undescended testicle suffers little before puberty and postponement of treatment, hormonal or surgical, until that time would therefore appear to be safe and would permit natural descent to occur in an appreciable number of cases At the time of puberty boys whose testicles are still undescended should be given a trial with hormone

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injections to be followed by surgery if unsuccessful.

It has been the editor's clinical observation in a large series of cases that hormonal therapy was of little, if any, use in causing an undescended testicle to descend. The vast majority of cases has been operated upon after puberty with fairly good results. This bears out the opinions of most of the careful clinical and experimental observers and until we know whether or not testes treated by hormones lose the power for spermatogenesis, the nonoperative treatment of undescended testes must be classified entirely in an experimental field and its use clinically applied with extreme caution and with full explanation to the parent or guardian Legal complications may arise otherwise.

Treatment by Operation—The operation of Torek seems to offer the best chances for correction of this condition. Some authorities believe that the operation should be done before the ninth year and the earlier the better. G. V. Foster³¹ regards the fourth year as the opportune time He gives as his reason that degeneration in the testicle does not begin before the fourth year. In the last 58 cases operated upon a change was made in 1 step of the Torek operation which is believed to have certain advantages over the original procedure

The Torek operation consists of exposing the undescended testicle through a herma incision and distending the scrotum with gauze. If a herma sac is present, it is attended to in the usual manner and the cord is cleared of its constituents, leaving only the spermatic vessels and vas deferens. The testicle is brought through the herma incision and placed on the inner aspect of the thigh, marking the place to which it is to be attached after passing through the scrotal wall. At this point on the thigh

a 1-inch incision parallel to the groin is made down to the fascia lata. The distended scrotum is then brought over to this incision and a similar incision made through the lower part of the scrotum. The gauze is removed from the scrotum and the upper skin margin of the thigh is sutured to the inner skin margin of the scrotal incision. This forms the back wall of the canal through which the testicle travels on its way to be sutured to the fascia lata. In the forming of this back wall, interrupted catgut sutures should be used, due to the difficulty of removing nonabsorbable sutures, and they should be placed in such a manner that the suture knot is on the skin surface and the thigh scrotal margins in proper coaptation to encourage union of the raw surfaces A small portion of the tunica propria of the testis is grasped by a hemostat, inserted through the scrotum and pulled down to the fascia lata of the thigh. Following Torek's technic, 2 catgut sutures are then placed through the testicular body and the testicle firmly sutured to the fascia lata of the thigh.

We have changed this technic in the last 58 cases for 2 reasons: The first is to obviate the possible testicular destruction caused by placing sutures through the body of the testicle; second, the internal saphenous vein is just underneath the pectineal portion of the fascia lata at the usual point of suture and we were fearful of plunging a needle through its walls and causing considerable hemorrhage. In our modification of this technic, a perpendicular incision is carefully made through this pectineal fascia about three-fourths of an inch in length. A continuous catgut suture is then placed along the margins of the fascia incision and left hanging loosely until the testicle is placed beneath it. When pulled tightly, the suture holds

the testicle firmly in place below this portion of the fascia lata The upper end of the incision should be left sufficiently free to admit the cord. In only a few of the 58 cases have we seen the internal saphenous vein when the fascia lata was opened, but this method is safer than pushing a needle blindly through the unopened fascia. In the second stage of the operation following our technic, the testicle showed not the slightest damage, and appeared smooth and glistening when delivered from beneath the fascia lata. The lower lip of the thigh incision is then sutured to the external lip of the scrotal incision by interrupted linen sutures. The inguinal incision is closed in the usual manner, and a piece of gauze is then run through the canal made by the scrotum and thigh and left there as a dressing The child is left in bed 6 to 8 days with his knees bound together in order that there may be as little pulling as possible on the suture line After 2 to 3 weeks full liberties are allowed. except cycling or horseback riding Since this hookup of scrotum to the thigh causes no pain, discomfort, or awkward gait, the components of the cord are thus allowed to stretch for 2 to 3 months before the second stage is done

The child is admitted to the hospital for only 24 to 48 hours for the second stage of the operation, which consists of releasing the hookup between the scrotum and thigh, reopening the fascia lata, and allowing the testicle to slip back into the scrotum. The thigh and scrotal incisions are then sutured in their normal positions. In bilateral nondescent of the testicles, only 1 testicle is placed in the thigh at the first operation, and at the second operation this testicle is released and the opposite testicle placed beneath its corresponding fascia lata. A third stage is necessary to complete the operation by releasing this testicle. The disadvantage of suturing both testicles to the thigh simultaneously is that inadvertent motions of the thigh might tear the sutures loose from the rudimentary scrotum.

PROSTATE

A great deal of work during the past few years has been done on the cause of prostatic hypertrophy. It is generally conceded that some disturbance in the glands which create internal secretions is the direct cause.

T. O. Powell³² has considered the following hormones, namely, male sex, female sex, the anterior pituitary gonadotrophic factor, and the anterior pituitarylike gonadotrophic hormones. of these hormones have been used in the treatment of various conditions, apparently without distributing the growth of the prostate. However, he reports a case of precocious prostatic hypertrophy following the treatment of undescended testes with commercial preparations of anterior-pituitarylike gonadotrophic hormones This occurred in a boy 17 years of age. Upon the discontinuance of the drug, the prostate apparently returned to normal size. The possibility of prostatic hypertrophy must be given serious consideration whenever these substances are being used in the treatment of other conditions

B Vidgoff^{3,3} reviewed all of the experimental work in the literature on the subject of hormonal influences in prostatic hypertrophy and says that the endocrine relationship is implied because man's sexual activity is sufficiently waning when prostatic hypertrophy becomes troublesome. The accidental finding of epithelial metaplasia in the prostate of animals after the injection of estrone has led to the theory that estrogenic dominance in a bisexual organ is the

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explanation of the clinical picture. The writer is not convinced that these findings are specific because it is well known that estrogenic substance has a general effect upon epithelial cells and the anatomical evidence does not support this theory. The reports of remarkable relief in the clinical picture of prostatic

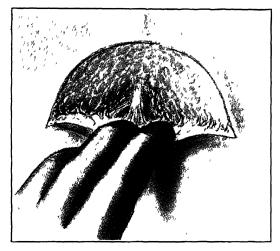


Fig 8 — Skin incision Superficial skin flap pulled down stretching fibers of median raphe before they are cut (Belt, Ebert and Surber · J Urol)

hypertrophy from the use of testosterone is not convincing because this substance causes a hypertrophy of the prostate and the clinical experimental work has been insufficiently controlled. The beneficial effects obtained are probably due to the effect on the congestion surrounding the adenomatous prostate and not because of any definite action of the There is evidence to adenoma itself suggest that the testis elaborates a substance which does have an inhibitory effect on the prostate but there is nothing specific to prove this statement and a great deal more work will be required. At the present time this then almost definitely rules out the rationale of the treatment of hypertrophy of the prostate by various hormonal substances and throws the treatment again back to the surgical amelioration of the symptoms caused by this pathological entity.

Control of Hemorrhage — Hemorrhage is one of the major complications of transurethral prostatic surgery and many methods have been devised to control it. F. C. Hendrickson³⁴ uses the following technic: At the end of the operation a Foley-Hendrickson hemostatic bag is passed into the bladder and inflated with 60 to 90 cc. of air. The capacity of this bag is large enough completely to fill the prostatic cavity in all excepting rare cases. All remaining blood clots are then washed out of the bladder. The contents of a small vial of hemostatic serum such as fibrogen for oral use, are instilled into the bladder through the catheter. The bladder is slightly inflated with about 30 cc. of air in order to permit movement of the



Fig 9—Finger in cleavage plane between external sphincter ani muscle and rectum. (Belt, Ebert and Surber J Urol)

bag inside the bladder By rapidly moving the bag in and out serum is worked down under the bag into the prostatic cavity. The bag is then drawn down into the wound and held under light traction for a half hour or more. The hemostatic

serum in the prostatic cavity quickly coagulates any fresh blood that flows from open vessels. The quick and tough clotting prevents escape of blood from under the bag and a tamponade results Therein lies the power of the hemostatic serum, namely, to produce tough blood

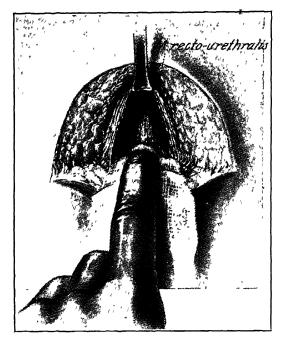


Fig. 10 — Finger depressing rectum disclosing fibers of recto-urethralis muscle. (Belt, Ebert and Surber J Urol)

clots under the bag. Use of this technic in about 100 resections has adequately demonstrated its efficiency. If, as rarely happens, bleeding continues, the clots can always be lavaged or sucked out through the noncollapsible thin-wall catheter incorporated in the Foley-Hendrickson hemostatic bag

Treatment of Hypertrophy—Gradually the rôle of transurethral prostatic surgery in the treatment of hypertrophy is resolving itself into the selection of the operation to fit the patient This has been emphasized very clearly by F. Hinman³⁵ who reserves transurethral surgery for sclerotic bladder necks, small median lobes and minor en-

largements of the gland, perineal prostatectomy being reserved more or less for the larger adenomas and carcinomas of the prostate. Since suprapubic prostatectomy, with its higher mortality, is the easiest operation, it is advocated for the use of those men not qualified by training and experience to approach the gland from the perineal route. Perineal prostatectomy, because of the dangers of the anal sphincter, the compression of the urethral muscle and the rectum itself, requires training, judgment and experience. That this danger is more theoretical than real is proven by the new perineal anatomical approach designed and advocated by E. Belt, C. E Ebert and A. C. Surber³⁶ who unhesitatingly approach the gland by retracting the external rectal sphincter

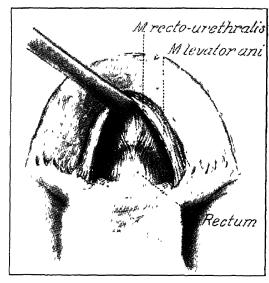


Fig 11 — External sphincter ani muscle lifted disclosing part of central tendinous plane of perineum, central fibers of rectourethralis muscle divided longitudinally in midline (Belt, Ebert and Surber J Urol)

Operation — A description of the operative procedure follows in which reference is made only to those anatomic structures actually encountered A spinal anesthetic is given. The patient is placed on a perineal table so constructed that

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an extreme lithotomy position is attained. In this position, the thighs are well flexed and separated, the buttocks are elevated and the upward tilted perineum comes to be parallel to the floor. The operative field, external genitalia and inside of both thighs are well scrubbed

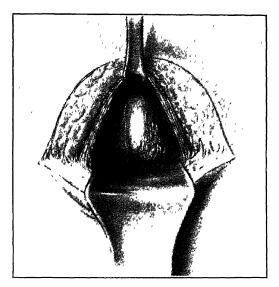


Fig 12 — Posterior retractor in place, fibers of recto-urethralis and levator ani muscles split by blunt dissection to disclose posterior layer of fascia of Denonvilliers (Belt, Ebert and Surber J. Urol)

with green soap, with water, and then with 1:10,000 bichloride.

With the aid of a syringe pressed against the external urinary meatus, about $6\frac{1}{2}$ ounces (200 cc) of $\frac{1}{2}$ per cent solution of meroxyl are allowed to traverse the urethra and flow into the bladder. This is done to effect a sterilization of the bladder contents. The skin of the perineum, perianal region, inside of both thighs, scrotum and pubis is painted with 1 · 1000 tincture of merthiolate The perineum is then draped with towels wet with 1 10,000 bichloride of mercury, leaving the operative site and external genitalia exposed A rubber dam is fastened to the perineum with skin clips in a manner which walls off the external anal aperture in order to

prevent contamination. A towel is fastened to the skin at the base of the scrotum with skin clips and then folded upward over scrotum and penis to leave only external urinary meatus exposed.

The incision through the skin is semicircular and placed on a radius about 1½ cm. from the anal mucosa running in effect from 1 ischial tuberosity to the other. The flap of skin thus released is depressed backward with the aid of a dry gauze sponge held against it beneath the fingers of the left hand.

The tension thus created causes the delicate fibers of the median raphe to stand out These are cut. Their release permits the handle of the knife to obtain an entrance by means of blunt dissection below the muscle fibers of the external anal sphincter.

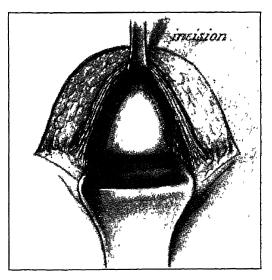


Fig 13—Levator ani muscles pushed laterally, rectum eased backward Posterior surface of prostate exposed. Dotted line marks incision through capsule. (Belt, Ebert and Surber J Urol)

These muscle fibers can be seen close to the skin of the lower flap. The fibers of the external anal sphincter separate very easily from the longitudinal fibers of the rectum, opening up a cleavage plane which is readily followed along the

longitudinal fibers to the apex of the prostate. Here the free anterior borders of the levator ani muscles run within a few millimeters of one another ("rectourethralis" muscle). The handle of the knife may be pressed between these bor-

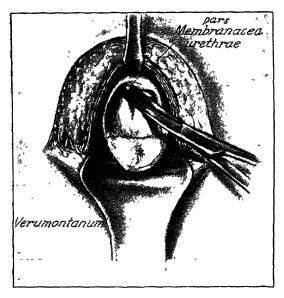


Fig. 14 — Scissors cutting membranous urethra off at junction with prostatic urethra (Belt, Ebert and Surber J Urol)

ders. With the left forefinger, the anal canal can be depressed

Lateral pressure is exerted against the borders of the levator ani muscles separating them widely. This movement exposes the tough fascia covering the posterior surface of the prostate

A number 24 French sound is passed through the external urmary meatus traversing the prostatic urethra and passing into the bladder. Forward and downward pressure against the handle of this sound helps to present the prostatic capsule into the wound and permits the posterior surface of the prostate to be more completely exposed. A posterior retractor placed over the rectum holds it down away from the operative field.

The prostatic capsule is entered through an inverted U-shaped incision, the transverse part of which is carefully placed in a point peripheral to the verumontanum.

This point is recognized as a soft spot which can be felt with the tip of the finger just proximal to the membranous urethra in the prostatic capsule. A flap thus formed is pressed backward carrying with it the verumontanum and the ducts leading from the seminal vesicles into the verumontanum. The ducts remain in the flap close to the prostatic capsule. A small triangle of urethra containing the verumontanum goes backward with the flap exposing the sound in the urethra The adenomatous nodules can be seen bulging into the prostatic urethra against the sound At their upper margins, within the apex of the gland, the urethra can be seen leaving the surface of the adenomatous lobes

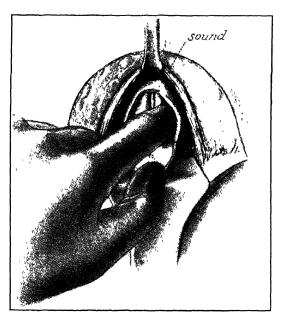


Fig 15—Lateral lobes of prostate shelled out of capsule (Belt, Ebert and Surber J Urol)

and passing toward the membranous urethra. This posterior (dorsal) aspect of the membranous urethra is carefully isolated and cut off with scissors

The adenomatous nodules are bluntly dissected from the compression capsule

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of the prostate with a sweeping motion of the finger which carefully keeps to the cleavage plane between adenoma and capsule.

The sound is then withdrawn, a number 24 F urethral catheter introduced through this urethral opening and the

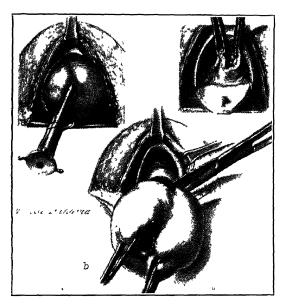


Fig 16—(a) Prostatic tractor inserted; (b) prostatic being cut from bladder neck; (c) prostate removed, bleeding from bladder neck controlled by Allis forceps (Belt, Ebert and Surber J Urol)

bladder contents (admixture of urine and meroxyl) evacuated, following which the catheter is discarded.

The remaining (anterior or ventral) portion of the membranous urethra is then divided, thus severing the urethra completely. Care is taken to leave as long a cuff of urethra as possible to facilitate its reconstruction later in the operation

The freeing motion is aided by means of a Markley prostatic tractor passed through the prostatic urethra into the bladder where it is opened to allow traction, and, as the lobes are mobilized, by thyroid clamps which pull the adenomatous nodules toward the operator. With them comes a cone of bladder neck

which is stripped backward by blunt dissection, carefully preserving the circular muscle fibers of the bladder neck which can be clearly seen. A cylinder of mucosa is finally reached which passes from the inner surfaces of the adenomatous masses to become continuous with the bladder mucosa. This tube is cut off with scissors. The first snick is made in the anterior portion and the bladder edge is at once grasped with an Allis clamp to keep it from retracting upward out of sight. Then the cut is extended around the entire circumference of the tube of urethra and the entire prostate thus freed

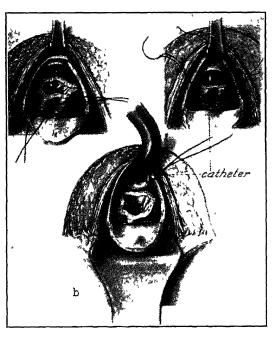


Fig 17—(a) Bleeders in bladder's neck are ligated, (b) rubber catheter inserted into urethra and retracted outward to facilitate placing first suture uniting anterior wall of urethra and bladder neck; (c) catheter then inserted into bladder and lateral and posterior walls of urethra are sutured to bladder neck (Belt, Ebert and Surber. J. Urol)

and removed. Often a large middle lobe necessitates carrying the cut high up transversely across the base of the trigone. Allis clamps are applied to each side of the bladder neck. The cone of bladder mucosa thus held in 2 Allis

clamps carries a rich blood supply coming down to it from the bladder. Often large spurting vessels can be seen within it. These arteries are sutured with number 2 chromic hemostatic ligatures passing through the bladder neck.

At times spurting vessels can be seen farther up on the side of the bladder

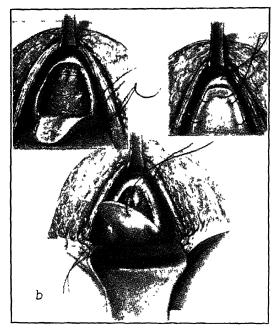


Fig. 18—(a) Membranous urethra and bladder neck united, sutures through capsule into bladder musculature to obliterate all dead spaces, (b) capsule being closed with interrupted sutures, (c) completion of closure (Belt, Ebert and Surber J Urol)

inside the capsule. These are similarly controlled When one is assured that there is no more bleeding from the bladder neck and inside the capsule, the neck of the bladder is examined to make sure that there are no remnants of adenomata or tags of tissue If any are present, they are carefully trimmed away. Following this a 2-hole urethral catheter, number 24 F in size, is introduced into the urethra through the penis and caused to emerge from the cut end of the urethra inside the capsule. It is then pulled out of the wound and held in an elevated position by a narrow anterior

retractor, revealing the cut end of the urethra. A number 2 chromic stitch is then taken through this anterior (ventral) border of the urethra, carried through the anterior (ventral) border of the bladder neck, tied and cut. After this procedure the free tip of the catheter is introduced into the bladder thus splinting the cut ends for anastomosis. A chromic stitch is taken on each side and 1 medially, completing the reconstruction of the urethra by its approximation to the bladder neck.

The closure of the prostatic capsule is the next step. In this procedure an

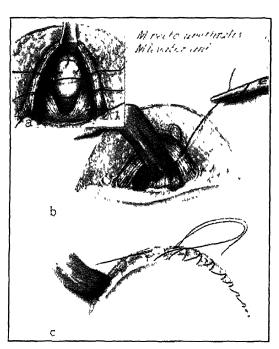


Fig 19—(a) Interrupted sutures bringing together recto-urethialis and levator ani muscles, (b) purse-string suture in sphineter ani externus, Peniose diain in space between capsule and rectum, (c) superficial fat and fascia brought together by continuous subcuticular stitch (Belt, Ebert and Surber J Urol)

attempt is made to close the dead space between the bladder and the capsule This is done by taking a stitch at each lower corner of the capsule, which includes some bladder tissue and emerges through the central flap. Five number 2 UROLOGY 1077

chromic sutures are usually necessary to approximate the flap and close the capsule. Thus the structures are brought back to their original anatomic position.

Three number 2 chromic stitches are taken in the fibers of the recto-urethralis and the medial portion of the pubococcygeal fibers of the levator ani muscles. A Penrose drain is placed in the space between the rectum and the capsule. The edge of the external sphincter anı muscle is approximated to the longitudinal fibers of the rectum with a pursestring stitch, number 2 chromic. Several interrupted plain catgut stitches close the superficial fascia. A continuous subcuticular running stitch closes the skin (plain catgut). Wound is dressed with moist compresses (hexyl-resorcinol, "S.T 37"), bladder irrigated, all clots removed and the catheter is strapped in place The patient is sent back to his room.

The Penrose drain is removed after 24 hours. Five per cent glucose in normal saline is given intravenously twice daily for 2 days, the catheter is irrigated frequently These patients are afebrile on the third postoperative day. At this time they are allowed to stand at the side of the bed for a few minutes, several times a day. A nonresidue diet is given for 1 week The bowels are moved (oil retention enema) about the sixth or eighth postoperative day The catheter is removed the eighth to twelfth postoperative day. Per priman healing is expected in 40 per cent of the cases Persistent sinuses are unknown length of hospitalization is from 10 to Most patients leave on the 21 days sixteenth postoperative day

URETER

Calculus

Much has been written as to the conservative and operative treatment of ureteral calculus, the diagnosis of which should be a comparatively easy one. Very often the calculus will show on a plain plate in an attempt to make a definite diagnosis between calculous disease and intra-abdominal conditions. A small percentage of calculi will not cast shadows on a plain x-ray film and if there is any question of doubt the patient should be cystoscoped and an attempt made to bring out the calculus by retrograde or intravenous pyelography. The vast majority of urinary calculi occurs between the ages of 20 and 50, and it should always be considered as a diagnosis in various types of abdominal pain where the picture is not clear cut. The vast majority of ureteral calculi occurs in the pelvic ureter and a fairly large percentage occur in the abdominal ureter and most of these cases are unilateral.

L. Herman and L. B. Greene³⁷ feel that every attempt should be made to dislodge the average small calculus in the ureter. However, where stones occur in the lower ureter and are the cause of repeated attacks of severe colic, they believe that open operation is the method of choice. In a general way, they give the following rules for operative interference

- 1 Repeated failure following the use of nonoperative measures.
 - 2 Impassable obstructions
- 3 Active renal infection whether antedating or succeeding instrumentation which cannot be controlled by indwelling catheters
- 4. Intolerance to or impossibility of ureteral instrumentation in cases of long standing calculous impaction in the ureter
- 5. Large calculi which from their size alone would not be expected to pass despite instrumentation.
 - 6. Excessive or uncontrollable pain
 - 7 Progressive renal dilatation

N. S. Moore,³⁸ in discussing this same subject, makes the statement that the popularity of open operation is rapidly on the increase and unhesitatingly operates where he feels that the stone is so large that it will not pass without permanent renal damage. He insists that in a conservative treatment of ureteral stones, gentleness of all manipulative procedures is the prime requisite.

Carcinoma

Carcinoma of the ureter is rather a common condition as a secondary involvement following carcinoma of the renal pelvis and there have been cases on record where tumors of the renal parenchyma have extended into and involved the ureter. These, of course, are secondary conditions and must be taken into consideration in the treatment of the primary disease.

E. Hess has devised a radon ureteral catheter for the secondary involvement of the ureter and has abandoned the use of the complete nephro-uretero-partial cystectomy in tumors of the renal pelvis. Where the general condition of the patient is such that it is inadvisable to do the extensive nephro-uretero-partial cystectomy, the ureteral stump is treated by the radon catheter after simple nephrectomy, with good results in several cases.

Primary carcinoma of the ureter is rather a difficult diagnosis to make A G Foord and P. A Ferrier 19 report 7 cases of primary carcinoma of the ureter. They noted in their cases, as well as 133 cases taken from the literature, that the primary tumors were most commonly found in the end of the ureter, many of them protruding into the bladder. The diagnosis is based on bleeding from 1 ureter, together with obstruction or a filling defect as shown by urogram, or by observation of a tumor protruding into the bladder. The treat-

ment of choice is *nephro-ureterectomy*. A 2-stage operation is much the safest. The prognosis is very bad, only 3 8-year cures having been reported.

Ureteral Spasm

Ureteral spasm very often causes severe coliclike pain which at times sımulates calculous disease. F S. Wetherell⁴⁰ feels that when the diagnosis of ureteral spasm is made and is unrelieved by all other measures and when the spasm can be localized in the lower half or two-thirds of the ureter, it will be relieved by a resection of the superior hypogastric plexus. The operation has become fairly well standardized but attention should be called to the necessity of a carefully conducted dissection which includes all of the finest fibriles, those communicating with the lumbar ganglia as well as those coursing over, and sometimes under, the common iliac arteries.

Transplantation of Ureters

E Hess⁴¹ in a complete discussion of the subject of transplantation of the ureters, uses a modification of the Himman technic with good results

Technic of Operation—The patient is prepared for several days with simple cleansing enemas Forty-eight hours before operation an ounce of castor oil is given About 6 hours before operation, the bowel is carefully irrigated with plain water. As soon as the abdomen is opened and the bowel is packed away, the anesthetic of choice being spinal, the sigmoid is clamped and the bowel is again carefully washed out with water until the washing becomes clear If there are any large pieces of feces in the bowel at that time they are flushed out through a proctoscope The ureter to be implanted is then dissected free without any attempt being made to strip it of its periureteral fascia and fat. It is cut off

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as near the bladder as possible. The bowel is then prepared according to the Coffey technic. Sutures are placed very much in the fashion that Hinman places his, first 3 sutures into the ureter through the submucosa and muscularis. The ureter is then obliquely cut after it has been fitted to the incision in the bowel, leaving about an inch to protrude into the lumen of the bowel. The bowel is blown up very gently with air and the mucosa is punctured with the cautery. Through this opening the ureter and the matchstick are plunged into the lumen of the bowel and manipulated until the matchstick disappears within the lumen when the sutures are tied holding the ureter to the submucosa and the muscularis. It may be advisable to put in 1 or 2 other sutures to hold the ureter in its bed as per the Hinman technic. The muscle is closed, usually with interrupted sutures over the ureter; one must make sure not to constrict the ureter when tying the sutures. A drain may or may not be placed in the cul-de-sac, depending upon the operator's judgment This is a simple speedy technic and offers the best chance for success.

All operations in this series were done by the Coffey catheter, the Coffey-Mayo, or the matchstick technic. Of those that survived, 2 were done by the Coffey catheter, 1 by the Coffey-Mayo and 3 by the matchstick technic

Conclusions—Transplantation of the ureters into the bowel as an operative procedure should be considered only when a condition exists which makes life sufficiently miserable that death is to be preferred. The operation, even with the simplest efficient technic, in the hands of the most skillful, is not without a very high mortality and morbidity. It is rarely indicated in cancer of the bladder and vesico-vaginal fistulae. It is more frequently indicated in the con-

tracted bladder due to the healing of a tuberculous cystitis, and in this class of patient there is a low mortality with very satisfactory symptomatic results. It is also indicated in intractable and incurable cases of interstitial cystitis. It is a valuable procedure in exstrophy of the bladder and epispadias, but should never be used in the adult exstrophy without a complete explanation of both its mortality and morbidity and should be an operation elected by the patient.

Since the completion of this paper a new technic has been described by Farrell and Lyman.42 This technic is described as an aseptic uretero-intestinal anastomosis. The operation was done on 7 dogs and all survived At the end of 6 months all but 2 dogs were killed and autopsied. The technic is modeled after the Eck fistula, an anastomosis of the portal vein and the inferior vena cava. While the procedure has given good results in this series of dogs, it apparently has never been applied clinically The technic seems to be rather difficult and time-consuming and the blind use of the silk ligature to create the opening in the ureter and bowel is not recommended. I can see no advantage over the Higgins technic, and believe that this new technic is even more difficult and complicated

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